Does psoriatic axial spondyloarthritis phenotype correlate with imaging morphotype?

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ABSTRACT

Objective. *To compare the magnetic resonance imaging (MRI) morphology of inflammatory and chronic lesions in the sacroiliac joints (SIJs) and spine between patients with non-psoriatic and psoriatic non-radiographic axial spondyloarthritis (axSpA and p-axSpA, respectively).*

Methods. *Patients from the EMBARK trial (NCT01258738) with axSpA (n=179) and p-axSpA (n=24) who had MRI data available were compared in terms of baseline demographics, clinical characteristics, and the frequency (n/N [%]) and distribution of inflammatory and structural SIJ and spinal lesions.*

Results. *Patients with p-axSpA were on average older (35.1 years vs. 31.7 years, p=0.047), had a higher occurrence of asymmetric sacroiliitis (54.2% vs. 29.6%, p=0.042), and a lower occurrence of human leukocyte antigen (HLA)-B27 positivity (41.7% vs. 73.7%, p=0.010) than patients with axSpA. There were no significant differences in the frequency of lesions in any of the SIJ or spinal quadrants between the two subgroups.*

Conclusion. *These data suggest that differences between axSpA and p-axSpA extend beyond presence of psoriasis, and include age, SI symmetry, and HLA-B27 status. These findings may help explain the morphotype-phenotype relationship across axSpA, similar to those described in older radiographic studies.*

Introduction

The Assessment of SpondyloArthritis International Society (ASAS) classifies spondyloarthritis (SpA) as axial SpA (axSpA) and peripheral SpA (1-3). Patients with axSpA can suffer permanent structural changes of the spine that result in progressive disability manifested as pain, fatigue, limited spinal mobility, impaired physical function, work disability, overall diminished health-related quality of life, and a high burden of disease (4, 5). Therefore, an accurate, early diagnosis is very important for the appropriate management of axSpA.

Diagnosis of axSpA depends on radiographic detection of sacroiliitis (SI) (1, 6). However, only 30% to 60% of patients diagnosed with early disease based on clinical criteria have radiographic SI (7), which may result in diagnostic delays of more than 12 years (8). Magnetic resonance imaging (MRI) can detect changes not visible by radiography, and has made possible establishment of non-radiographic axSpA (nr-axSpA) as a category (9). Despite this, nr-axSpA remains under-reported (10). The magnitude of the pathologic changes in the axial skeleton is used to quantify inflammatory and structural outcomes in clinical trials in axSpA (11, 12). Certain differences between non-psoriatic and psoriatic SpA – for example, bilateral and unilateral SIJ bone marrow oedema, respectively – have been observed in clinical practice (Fig. 1).

However, to the best of our knowledge, there were no systematic attempts to correlate clinical manifestations (phenotype), such as the presence of psoriasis, with MRI evaluations of the spine and SIJ (morphotype) in patients with axSpA without radiographic damage.

In this *post hoc* analysis of a trial conducted in individuals with nr-axSpA (EMBARK), we compared patients with and without psoriasis in terms of demographic and clinical characteristics, including the symmetry of sacroiliitis (SI) and the distribution of lesions in the SI and the spine.

Methods

Patients

This post hoc analysis used baseline MRI data from patients without psoriasis (denoted, for simplicity, as axSpA) and with psoriasis (p-axSpA) from the EMBARK trial (NCT01258738). EMBARK was a randomised, double-blind, two-period, multicentre phase 3b study conducted in 14 countries in Europe, Asia, and South America that compared the efficacy and safety of etanercept *versus* placebo in patients with active nr-axSpA (classified using the ASAS criteria: symptom duration >3 months and <5 years; Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] ≥4 at screening) (13). The first MRI was performed prior to the initial dosing with the study drug. All MRIs were conducted locally and

assessed by central reading. Psoriasis at baseline was assessed locally, by trial investigators.

The study protocol was approved by the relevant ethics committees in participating countries or institutions.

Analyses

The subgroups with axSpA and p-axSpA were compared in terms of baseline demographic and clinical characteristics, including the occurrence of SIJ inflammation, structural lesions, spinal inflammatory lesions, and distribution of symmetric and asymmetric SI. Symmetric SI was defined as both left and right Spondyloarthritis Research Consortium of Canada (SPARCC) SIJ score ≥2. Asymmetric SI was defined as either left or right SPARCC SIJ score ≥2 and the other SPARCC SIJ score <2. Non-SI was defined as both left and right SPARCC SIJ scores <2.

The subgroups were also compared in terms of occurrence of baseline SPARCC SIJ lesions >0 (SIJ inflammation >0) in the four SIJ quadrants (lower iliac, upper iliac, lower sacral, or upper sacral) and the four spinal quadrants (upper anterior, lower anterior, upper posterior, or lower posterior). Spinal quadrants were assessed by scoring the anterior vertebral edge of each vertebra between the lower edge of the second cervical vertebra (C2) and the upper edge of the first thoracic vertebra (T1), and between the lower edge of the twelfth thoracic vertebra (T12) and the upper edge of the first sacral vertebra (S1).

Continuous parameters were analysed using one-way analysis of variance. Categorical parameters were analysed using Fisher exact test, except for the SI symmetry distribution and the SIJ/spinal quadrant analysis, which were performed using the Cochran-Mantel-Haenszel test. Because of the *post hoc* nature of these analyses, there were no corrections for multiple hypothesis testing.

Table I. Baseline demographic and clinical characteristics.

Characteristic	Non-psoriatic axSpA n=179	Psoriatic axSpA n=24	*p*-value
Age, mean (SD), y	31.7 (7.7)	35.1 (7.7)	**0.047**
Male, n (%)	105 (58.7)	16 (66.7)	0.512
Race, n (%)			
White	128 (71.5)	22 (91.7)	0.244
Asian	40 (22.4)	2 (8.3)	
Other	11 (6.1)	0	
BMI, Mean (SD), kg/m^2	25.1 (4.5)	25.2 (4.4)	0.893
Symptom duration, Mean (SD), y	2.4 (1.9)	2.9 (1.5)	0.211
Dactylitis, n (%)	12 (6.7)	3 (12.5)	0.396
Enthesitis, n (%)	78 (43.6)	12 (50.0)	0.663
SI type, n (%)			
Symmetric	63 (35.2)	4 (16.7)	**0.042**
Asymmetric	53 (29.6)	13 (54.2)	
Non-SI	63 (35.2)	7 (29.2)	
Total SPARCC MRI SIJ score			
Mean (SD)	7.5 (9.3)	8.1 (10.3)	0.756
Median	3.5	3.3	
(min, max)	(0.0, 48.5)	(0.0, 41.0)	
≥2, n (%)	122 (68.2)	19 (79.2)	0.349
Left SPARCC SIJ score			
Mean (SD)	3.8 (5.6)	2.9 (4.6)	0.429
Median	2.0	1.0	
(min, max)	(0.0, 28.5)	(0.0, 18.0)	
≥2, n (%)	91 (50.8)	10 (41.7)	0.515
Right SPARCC SIJ score			
Mean (SD)	3.6 (5.4)	5.2 (7.1)	0.201
Median	1.5	1.3	
(min, max)	(0.0, 27.0)	(0.0, 23.0)	
≥2, n (%)	88 (49.2)	11 (45.8)	0.830
SPARCC MRI 6 DVU spinal score			
Mean (SD)	4.2 (6.4)	2.3 (2.9)	0.153
Median	1.5	1.0	
(min, max)	(0.0, 38.7)	(0.0, 9.3)	
≥2, n (%)	84 (46.9)	10 (41.7)	0.669
SPARCC MRI 23 DVU spinal score			
Mean (SD)	4.6 (8.5)	2.7 (4.2)	0.260
Median	1.5	1.0	
(min, max)	(0.0, 64.3)	(0.0, 18.3)	
≥2, n (%)	84 (46.9)	10 (41.7)	0.669
HLA-B27 positive, n (%)	132 (73.7)*	10 (41.7)†	**0.010**

axSpA: axial spondyloarthritis; BMI: body mass index; DVU: discovertebral unit; HLA: human leukocyte antigen; MRI: magnetic resonance imaging; p-axSpA: psoriatic axial spondyloarthritis; SD: standard deviation; SIJ: sacroiliac joint; SPARCC: Spondyloarthritis Research Consortium of Canada. *n=176, †n=22.

Results

There were 179 patients with non-psoriatic axSpA and 24 patients with p-axSpA who had MRI data available. At baseline, the subset of patients with p-axSpA was on average older (p=0.047), had a more uneven distribution of symmetric and asymmetric SI, which was skewed toward asymmetry (p=0.042), and a significantly lower proportion of individuals positive for human leukocyte antigen (HLA)–B27 (p=0.010) (Table I). There were no significant differences in SPARCC scores for the SIJ or spine (Table I), or in the measures of erosions, fat metaplasia, or ankylosis (data not shown).

In addition, there were no significant differences between patients with axSpA and p-axSpA in the proportions of patients with SIJ or spinal lesions in each of the four SIJ or spinal quadrants, respectively (Table II). An analysis by SIJ and spinal quadrants suggests that there were significant differences in the distribution of SPARCC SIJ lesions (occurrence range: 52–78%) and spinal lesions (36–51%) in patients with axSpA, with similar but not significant differences in distribution in those with p-axSpA (Table II).

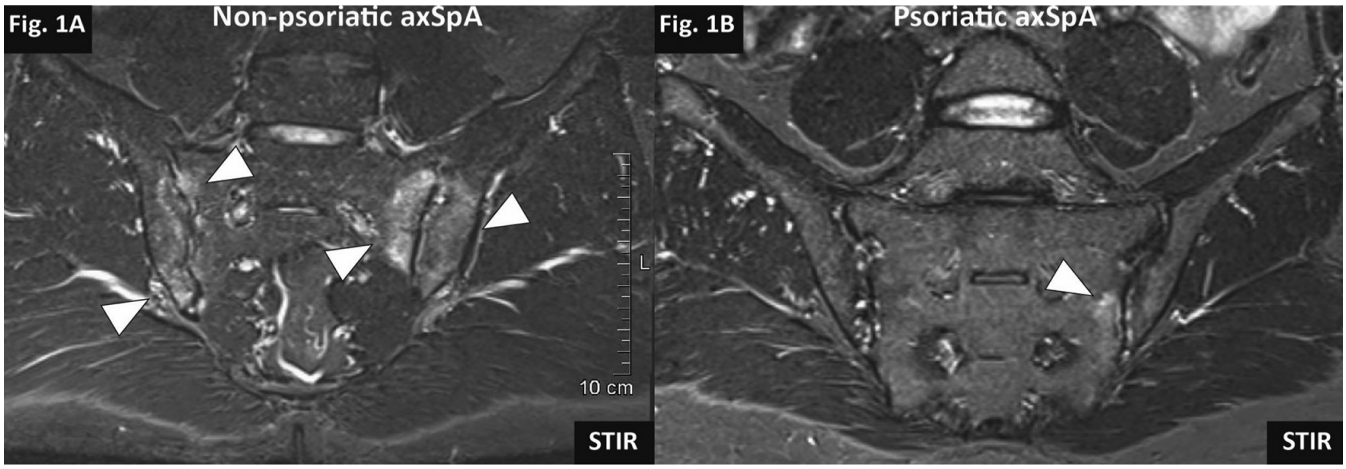

Fig. 1. MRI evidence of bilateral and unilateral SIJ bone marrow oedema in patients with non-psoriatic and psoriatic axSpA (images courtesy of X. Baraliakos) Typically, bone marrow oedema (arrowheads) appears bilaterally and with larger extent in patients with non-psoriatic axSpA, and unilaterally with less extent in patients with psoriatic axSpA. axSpA: axial spondyloarthritis; MRI: magnetic resonance imaging; STIR: short tau inversion recovery.

Table II. Frequency of SPARCC SIJ (by SIJ quadrant) and spinal lesions (by spine quadrant) at baseline, n (%).

	Non-psoriatic axSpA n=176	Psoriatic axSpA n=24	*p*-value
SIJ quadrant			
Upper iliac	92 (52.3)	13 (54.2)	0.862
Lower iliac	138 (78.4)	19 (79.2)	0.933
Upper sacral	104 (59.1)	17 (70.8)	0.271
Lower sacral	99 (56.3)	16 (66.7)	0.334
Overall	158 (89.8)	22 (91.7)	0.772
p-value between four quadrants	**<0.001**	0.316	
Spine quadrant			
Upper anterior	89 (50.6)	8 (33.3)	0.114
Lower anterior	82 (46.6)	10 (41.7)	0.651
Upper posterior	71 (40.3)	9 (37.5)	0.790
Lower posterior	64 (36.4)	6 (25.0)	0.275
Overall	132 (75.0)	15 (62.5)	0.194
p-value between four quadrants	**0.035**	0.660	

axSpA: axial spondyloarthritis; SIJ: sacroiliac joint; SPARCC: Spondyloarthritis Research Consortium of Canada.

Discussion

In this brief report, our goal was to identify clinical and imaging characteristics that could help distinguish non-psoriatic from the psoriatic phenotype in non-radiographic axSpA. To the best of our knowledge, this is the first attempt at such an analysis, and comparisons of our data with the extant literature are sparse. Of note, the lower occurrence of HLA-B27 in the psoriatic *versus* non-psoriatic subset is in agreement with observations from the DESIR cohort, which recruited patients with recent-onset axSpA (14). It is also in agreement with differences in HLA-B27 prevalence between psoriatic and non-psoriatic phenotypes of patients with radiographic SpA (15), which suggests that our observation is not an artefact of group selection or of a small study sample. The findings about the distribution of SIJ and spinal lesions in patients with and without psoriasis (Table II), although intriguing, are less reliable, because there are no published reports that investigated this difference, there is no suggestion of biologic underpinnings of this potential phenomenon, and the absence of *p*-values below 0.05 in the subgroup with psoriatic axSpA may be a reflection of a low number of patients.

Key limitations of this analysis are its *post hoc* nature and the small sample size in the p-axSpA subgroup. Nonetheless, the observed differences in patients' age, SI symmetry, and HLA-B27 positivity suggest a distinct pattern of inflammation in patients with axSpA and concomitant psoriasis. These observations may be useful in daily clinical practice and research, as they could lead to an improved diagnostic accuracy, and ultimately aid physicians in determining the optimal management strategy for their patients. Prospective long-term studies are warranted to validate these findings.

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Data sharing

Upon request, and subject to certain criteria, conditions and exceptions (see https://www.pfizer.com/science/clinical-trials/trial-data-and-results for more information), Pfizer will provide access to individual de-identified participant data from Pfizer-sponsored global interventional clinical studies conducted for medicines, vaccines and medical devices (1) for indications that have been approved in the US and/or EU or (2) in programmes that have been terminated (*i.e.* development for all indications has been discontinued). Pfizer will also consider requests for the protocol, data dictionary, and statistical analysis plan.

Data may be requested from Pfizer trials 24 months after study completion. The de-identified participant data will be made available to researchers whose proposals meet the research criteria and other conditions, and for which an exception does not apply, via a secure portal. To gain access, data requestors must enter into a data access agreement with Pfizer.

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