

## Editorial

### Immunology, Allergic Disorders & Rheumatology



# How Should We Classify Patients Who Have Spondylitis and Psoriasis?

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Ankylosing spondylitis/axial spondyloarthritis (AS/axSpA) is a chronic inflammatory disease that affects the sacroiliac joints and spine, causing back pain and stiffness, and disability. It often accompanies peripheral arthritis, enthesitis, or extra-musculoskeletal manifestations. Psoriasis is a typical co-morbid skin disease in 10% of AS/axSpA patients. The cumulative frequency of psoriasis increased to 27% with an incidence of 2.1/100 patient-years in the patients with recent axSpA.<sup>1</sup> Psoriasis has altered the expression and treatment of axSpA to more peripheral arthritis and increased use of methotrexate or biologic agents.

Meanwhile, since psoriatic arthritis (PsA) was defined by Moll and Wright in 1973, various forms of PsA, including spondylitis, oligoarthritis, polyarthritis and others, have been described. PsA shares various clinical features with AS/axSpA and has been classified as part of spondyloarthritis by several criteria, including the recent Assessment of Spondyloarthritis International Society (ASAS) criteria. However, the PsA also has independent classification criteria originally proposed by the Classification Criteria for Psoriatic Arthritis (CASPAR) group in 2006. Axial involvement of PsA, referred to as psoriatic spondylitis or axial PsA (axPsA), is very frequent and has been observed in 50% of Korean patients with PsA.<sup>2</sup> Men, HLA-B27 positivity, and elevated CRP are more common, and disease activity, function and overall health indices are worse in axPsA than in peripheral PsA.

Given that both criteria are currently popular, patients with concurrent spondylitis and psoriasis may be classified as AS/axSpA and/or PsA at the discretion of physicians. However, it is not clear whether axPsA is the same disease as AS/axSpA with psoriasis or another disease distinct from AS/axSpA although they appear to have certain features in common. The clarified classification of AS/axSpA or axPsA was not clinically significant because treatment options for both diseases were limited. As the clinical trials of drugs for PsA were conducted mainly in patients with peripheral PsA, the pharmacological treatment of axPsA was extrapolated from that of AS/AxSpA. This assumed that axSpA and AS/axSpA might be the same diseases.

Lately, various new drugs such as cytokine inhibitors and small molecules targeting pathogenesis have been introduced to treat PsA or AS/axSpA and some of them suggest the difference in treatment response between two diseases. In particular, ustekinumab, IL-12/23 p40 monoclonal antibody, which was ineffective in AS, was reported to reduce axial symptoms and disease activity in the patients with axPsA by post-hoc analysis.<sup>3</sup> Systemic

corticosteroids reduced disease activity significantly much more in axPsA than in AS/axSpA. The above indicates that axPsA and AS/axSpA may be distinct conditions.

In addition to response to certain drugs, there are remarkable differences between axPsA and AS/axSpA in genetic, clinical, and imaging aspects.<sup>4</sup> The patients with axPsA have a lower frequency of male and HLA-B27 than those with AS/axSpA. The age of onset is older and inflammatory back pain less common, but peripheral arthritis more frequent in axPsA. Some radiographic features differ: less severe, frequently asymmetrical sacroiliitis, more common cervical spine involvement, non-marginal, thick syndesmophytes and paravertebral ossification in axPsA vs AS/axSpA.

The difference between axPsA and AS/axSpA was also demonstrated from recently published Korean data where Kim, et al.<sup>5</sup> analyzed the baseline characteristics of PsA and AS patients registered in KOBIO (Korean College Rheumatology Biologics & Targeted therapy registry). Compared to AS patients with psoriasis, the frequency of male (78% vs. 56%), HLA-B27 positivity (76% vs. 21%), and uveitis (32% vs. 0%) was lower, but that of peripheral arthritis was higher (34% vs. 63%.) in the patients with psoriatic spondylitis, although its definition is unclear, just the physician reported. These findings are comparable to existing studies of foreign countries.

Comparative data between axPsA and AS/axSpA to date need to be further validated as the definition of axPsA and outcome parameters were not consistent in most previous studies. When axPsA was often defined by radiographs, 25% of patients had no symptoms; it is unknown if these patients have clinical significance. Degenerative change in the axial skeleton associated with older axPsA patients might affect cohort enrollment and evaluation. Therefore, a larger, long-term study is required to determine the consensual definition, classification and outcome parameters of axPsA. ASAS and GRAPPA (Group for Research and Assessment of Psoriasis and Psoriatic Arthritis) are now conducting this joint research, known as AXIS (Axial Involvement in Psoriatic Arthritis).

The patients who have both spondylitis and psoriasis can be dissected into distinct conditions, including AS/axSpA with psoriasis as an extra-musculoskeletal event, inflammatory axial involvement in the context of PsA, overlap syndrome which exhibits the features of both axPsA and AS/axSpA at the same time, or degenerative axial disease which occurs accidentally in patients with psoriasis. To distinguish between these conditions, a thorough clinical investigation of back pain and appropriate imaging will be required. Up to the establishment of clear criteria for the definition and classification of axPsA, clinicians should keep several possibilities in mind not to be trapped in closed judgments when diagnosing patients with spondylitis and psoriasis.

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