

The Definition and Measurement of Axial Psoriatic Arthritis

Ennio Lubrano, Wendy Joanne Parsons, Antonio Marchesoni, Ignazio Olivieri, Salvatore D'Angelo, Alberto Cauli, Francesco Caso, Luisa Costa, Raffaele Scarpa, and Luca Brunese

ABSTRACT. This review seeks to update the state of the art of axial psoriatic arthritis (axPsA). The definition and assessment of axPsA can be problematic because no agreement and no definitive data on this topic have been published, resulting in uncertainty as to the best approach to deal with these patients. A few recent scientific reports show new data on the possible coincidence of diffuse idiopathic skeletal hyperostosis and axPsA, as well as on the radiological assessment as measured with the validated instruments for axPsA. Moreover, the role of magnetic resonance imaging has also been evaluated for this intriguing subset. All data confirmed that radiological assessment is a useful tool to detect typical findings of axPsA, while other imaging techniques remain to be validated. Finally, there is no evidence to support treatment of axPsA with traditional disease-modifying antirheumatic drugs, while a "leap" to biologic agents is the only treatment after failure with nonsteroidal antiinflammatory drugs. (J Rheumatol Suppl. 2015 Nov;93:40–2; doi:10.3899/jrheum.150634)

Key Indexing Terms:

PSORIATIC ARTHRITIS AXIAL INVOLVEMENT RADIOGRAPHIC SCORING METHODS
BATH ANKYLOSING SPONDYLITIS RADIOLOGY INDEX
MODIFIED STOKES ANKYLOSING SPONDYLITIS SPINE SCORE
PSORIATIC ARTHRITIS SPONDYLITIS RADIOLOGY INDEX

From the Academic Rheumatology Unit, Department of Medicine and Health Sciences, University of Molise, Campobasso; Rheumatology Department, Istituto Ortopedico G. Pini, Milan; Rheumatology Department of Lucania, "S. Carlo Hospital," Potenza and Madonna Delle Grazie Matera, Potenza and Matera; Rheumatology Unit, Department of Medical Sciences, University of Cagliari, Cagliari; Rheumatology Unit, Department of Medicine DIMED, University of Padua, Padua; and Rheumatology Unit, Department of Clinical Medicine and Surgery, University Federico II, Naples, Italy.

E. Lubrano, MD, PhD, Aggregate Professor of Rheumatology, Academic Rheumatology Unit, Department of Medicine and Health Sciences, University of Molise; W.J. Parsons, BSc, MPH, Medical Statistician, Academic Rheumatology Unit, Department of Medicine and Health Sciences, University of Molise; A. Marchesoni, MD, Consultant Rheumatologist, Rheumatology Department, Istituto Ortopedico G. Pini; I. Olivieri, MD, Consultant Rheumatologist and Head of Rheumatology Department, Rheumatology Department of Lucania, "S. Carlo Hospital," and Madonna Delle Grazie Matera; S. D'Angelo, MD, Consultant Rheumatologist, Rheumatology, Department of Lucania, "S. Carlo Hospital," and Madonna Delle Grazie Matera; A. Cauli, MD, PhD, Aggregate Professor of Rheumatology, Rheumatology Unit, Department of Medical Sciences, University of Cagliari; F. Caso, MD, PhD, Rheumatology Unit, Department of Medicine DIMED, University of Padua; L. Costa, MD, Assistant Professor of Rheumatology, Rheumatology Unit, Department of Medicine DIMED, University of Padua; Rheumatology Unit, Department of Clinical Medicine and Surgery, University Federico II; R. Scarpa, MD, Associate Professor of Rheumatology and Head of Rheumatology Department, Rheumatology Unit, Department of Clinical Medicine and Surgery, University Federico II; L. Brunese, MD, Chair and Professor of Radiology, Department of Medicine and Health Sciences, University of Molise.

Address correspondence to Prof. E. Lubrano, Department of Medicine and Health Sciences, University of Molise, Campobasso, Italy; E-mail: ennio lubrano@hotmail.com

The definition and measurement of axial disease in psoriatic arthritis (axPsA) remains problematic¹. Criteria proposed for

recognition of axPsA vary from an isolated unilateral grade 2 sacroiliitis to those used for ankylosing spondylitis (AS)². As a consequence of this broad spectrum of proposed criteria, the prevalence of axPsA ranges from 25% (early disease and based only on clinical assessment) to 75% (late disease and sophisticated imaging)³.

Regarding clinical course, axPsA is usually less severe than AS, and in many respects it is dissimilar, mainly in the radiological patterns of the disease^{2,3}. In particular, axPsA shows radiographic features such as asymmetrical sacroiliitis, nonmarginal and asymmetrical syndesmophytes, paravertebral ossification, and frequent involvement of the cervical spine. These features are potentially helpful in diagnosing PsA and differentiate it from some cases of psoriasis with coincidental AS^{4,5}. An intriguing clinical and radiological issue raised in the last few years is the possible coincidence of DISH (diffuse idiopathic skeletal hyperostosis). To address this interesting and challenging topic, one report shows that DISH can be present in patients with PsA and was associated with older age and high body mass index (BMI)⁶. Moreover, the authors showed that DISH and axPsA can coexist in some patients⁶. With regards to imaging assessment of axPsA, at present radiological evaluations seem to be the main approach, even if some imaging studies assessed axial involvement of patients with PsA using magnetic resonance imaging (MRI). This led us to consider an update on the management of axPsA. The present review reports on recent scientific contributions to this topic by updating the literature of the last 5 years.

Of particular interest is a report on the possible coincidence

of DISH (diffuse idiopathic skeletal hyperostosis) and axPsA⁶. This study assessed the prevalence of DISH, any association with clinical and/or other factors (i.e., sex, BMI, etc.), and the possibility of coincidence of the 2 conditions. The results showed that DISH was recognized in 78 out of 938 patients with PsA (prevalence 8.3%), and DISH was associated with older age and high BMI. The authors concluded that DISH and axPsA can coexist in some patients with PsA⁶.

Another study compared the discriminative ability of the Ankylosing Spondylitis Disease Activity Score and the Bath Ankylosing Spondylitis Disease Activity Index in a group of patients with axPsA⁷. The study showed that both instruments have similar discriminative ability in the assessment of disease activity in axPsA⁷. Indeed, the measurement of disease activity is complicated in axPsA because some patients can have spinal radiological involvement but be clinically asymptomatic⁸.

One of the main characteristic aspects of axPsA is the radiological pattern, which is distinguishable from that of AS and other inflammatory or mechanical spinal disorders.

The nontypical radiological pattern of axPsA, compared to that classically observed in patients with AS, was first described by McEwen, *et al*⁴ and later by Helliwell, *et al*⁵. The 2 studies describe a radiological picture with certain peculiarities. Similar results were later confirmed by other authors⁹. In fact, sacroiliac joint involvement is not so frequent and is found mainly as asymmetrical in axPsA compared to AS. This finding was confirmed in a validation study in which axial involvement at the cervical and lumbar spine without sacroiliac involvement was observed in 7/71 patients by the Bath AS Radiology Index (BASRI; 9.8%) and in 3/70 by modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS; 4.28%)¹⁰.

Another radiological finding distinguishing axPsA from AS is the type of syndesmophytes. In fact, since the studies by McEwen, *et al*⁴ and Helliwell, *et al*⁵, nonmarginal and asymmetrical syndesmophytes with a so-called “chunky” shape were found in patients with axPsA. These syndesmophytes had a substantial structural difference to those “coarse” marginal and symmetrical ones observed in classic AS. The radiological patterns of axPsA might be completely different qualitatively from those observed in patients with AS. Even the distribution along the spine is not similar to that seen in AS, in which a progression of syndesmophytes from lumbar toward cervical is the rule, while a more random distribution is the most frequent finding in axPsA. Indeed, sometimes the type of syndesmophytes occurring in patients with axPsA could be so “atypical” that they are quite difficult to distinguish from those occurring in AS, as well as those in patients with osteoarthritis. One study proposed to differentiate the 2 main radiological findings (syndesmophytes and spondylophytes) by using a 45°-angle cutoff on lateral views¹¹. The syndesmophytes grow at an angle of < 45° to the vertebral edge, while spondylophytes grow at an angle of > 45° to the vertebral edge¹¹. In this way it is possible to separate, to a certain extent, the inflammatory

radiological findings from those that are truly degenerative.

Another aspect commonly observed in clinical practice is the frequent involvement of the zygoapophyseal joints at the cervical spine, with a tendency in some patients to be the only anatomical area of the vertebrae to be involved. The radiological scoring systems developed and validated for AS do not take into account the posterior elements of the spine. This, in turn, would not help in detecting true cervical involvement in axPsA, biasing the identification of damage. This interesting and peculiar finding was confirmed in a study in which 22/77 patients (28%) showed fusion of the zygoapophyseal joints at the cervical spine, but this radiological finding is not a criterion according to the radiological scoring system for AS¹⁰.

Initial studies by McEwen, *et al*⁴ and Helliwell, *et al*⁵ led to reevaluation of the radiological assessment of axPsA. To address this topic, a study was performed to validate the existing scoring instruments (BASRI and mSASSS^{12,13}) in a group of patients with axPsA¹⁰. The study evaluated PsA patients with established disease and axial involvement. Inclusion criteria were the presence of clinical spinal involvement (inflammatory back pain according to Calin criteria) and/or radiological axial involvement¹⁰. The study showed, in a group of 77 patients with established disease and axial involvement, that the 2 radiological instruments were found to be valid and feasible. Both were easy to use and took little time to complete, had good test-retest reliability, and both showed modest but significant correlations with anthropometric measures of spinal involvement in this disease. The results were obtained from real clinical practice, giving a picture of a typical patient with established axPsA. However, a weakness of these 2 scoring systems in detecting the axPsA is that the BASRI assumed at least grade 2 sacroiliitis, and in many patients with axPsA, spinal involvement without sacroiliac joint involvement is possible. On the other hand, mSASSS is characterized by frequent missing data, takes longer to be performed, and is not very practical in daily clinical practice. Thus, neither BASRI nor mSASSS take into account in their scores the zygoapophyseal joints. As mentioned, the frequent cervical involvement in axPsA needs to be detectable, but the 2 scoring systems do not encompass these radiological features of axPsA.

Therefore we undertook to design a radiological score tailored for axPsA. A new index, the PASRI (Psoriatic Arthritis Spondylitis Radiology Index), was developed¹⁴. The index has been shown to encompass a greater range of the spinal radiological features of PsA and is a valid instrument with a good correlation with anthropometric measures and patient-reported outcome measures. Moreover, the PASRI has the advantage over existing instruments (i.e., BASRI and mSASSS) for its capacity to detect posterior axial involvement¹⁴.

Following these studies, other groups reported results on radiological involvement of axPsA. In particular, Biagioni, *et al*, recently developed a computerized scoring application and compared the intra- and the inter-rater reliability of these

scoring systems in AS and axPsA¹⁵. The results of this validation study showed that the available scoring systems performed well in AS and have moderate intra- and inter-rater reliability when applied to axPsA. However, the PASRI may be superior for assessing structural damage in axPsA¹⁵.

In terms of other imaging studies, a few years ago an MRI study on axPsA assessed the prevalence of bone edema in symptomatic axPsA and compared this prevalence with that in nonradiographic axial spondyloarthritis and AS, as well as a possible relationship with HLA-B27 status¹⁶. Results showed that HLA-B27 positivity defined a group of patients with more severe axial bone edema that is likely related to the classic AS phenotype. On the other hand, HLA-B27-negative PsA was more likely to be reported as a “negative” MRI result¹⁶. These results are, to a certain extent, in keeping with the different pathophysiology of PsA compared to AS, supporting the concept that among the spondyloarthritides some entities should be considered separately but under the same umbrella. Moreover, the role of conventional radiology in axPsA for qualitative and quantitative evaluations is still crucial.

Treatment of axPsA remains a challenge for the rheumatologist¹⁷. Traditional disease-modifying antirheumatic drugs (DMARD) did not show any efficacy in axial involvement, while for peripheral subsets, a condition of remission is even possible¹⁸. On the other hand, in true axial involvement various recommendations showed that after NSAID and physiotherapy, in case of failure, biologic agents are the way forward. For instance, the Recommendations of the Italian Society for Rheumatology are in keeping with these treatment strategies¹⁹. In fact, a study to assess the effectiveness of a biologic agent in axPsA was carried out showing a good response at 12 months’ therapy²⁰.

Only a few reports have been found in the present update on axPsA. However, results obtained still support the identity of axPsA, clinically, radiologically, and even based on MRI findings. Moreover, radiological assessment should be considered the gold standard for the identification of qualitative and/or quantitative findings to distinguish axPsA from DISH, AS, and other degenerative/or inflammatory conditions.

AxPsA, therefore, must be considered as an intriguing subset of an intriguing disease, one that deserves careful investigation to achieve better characterization and treatment. Finally, as a research agenda, further studies are both welcome and necessary to identify instruments tailored to axPsA.

ACKNOWLEDGMENT

This review article is dedicated to the memory of Professor Antonio Spadaro, who was also a member of GRAPPA. He was a scientist and a respected and beloved physician of the Sapienza University of Rome.

REFERENCES

1. Lubrano E, Marchesoni A, Olivieri I, D’Angelo S, Palazzi C, Scarpa R, et al. The radiological assessment of axial involvement in psoriatic arthritis. *J Rheumatol Suppl*. 2012 Jul;89:54-6.
2. Gladman DD. Axial disease in psoriatic arthritis. *Curr Rheumatol Rep* 2007;9:455-60.
3. Lubrano E, Spadaro A. Axial psoriatic arthritis: an intriguing clinical entity or a subset of an intriguing disease? *Clin Rheumatol* 2012;31:1027-32.
4. McEwen C, Di Tata D, Lingg C, Porini A, Good A, Rankin T. A comparative study of ankylosing spondylitis and spondylitis accompanying ulcerative colitis, regional enteritis, psoriasis and Reiter’s disease. *Arthritis Rheum* 1971;14:291-318.
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. Haddad Amir, Thavaneswaran A, Toloza S, Chandran V, Gladman DD. Diffuse idiopathic skeletal hyperostosis in psoriatic arthritis. *J Rheumatol* 2013;40:1367-73.
7. Kilic G, Kilic E, Nas K, Karkucak M, Capkin E, Dagli AZ, et al. Comparison of ASDAS and BASDAI as a measure of disease activity in axial psoriatic arthritis. *Clin Rheumatol* 2015;34:515-21.
8. Palazzi C, Lubrano E, D’Angelo S, Olivieri I. Beyond early diagnosis: occult psoriatic arthritis. *J Rheumatol* 2010;37:1556-8.
9. Jacobson JA, Girsh G, Jiang Y, Resnick D. Radiographic evaluation of arthritis: inflammatory conditions. *Radiology* 2008;248:378-89.
10. Lubrano E, Marchesoni A, Olivieri I, D’Angelo S, Spadaro A, Parsons WJ, 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* 2009;27:977-80.
11. Baraliakos X, Listing J, Rudwaleit M, Haibel H, Brandt J, Braun J, et al. Progression of radiographic damage in patients with ankylosing spondylitis: defining the central role of syndesmophytes. *Ann Rheum Dis* 2007;66:910-5.
12. MacKay K, Mack C, Brophy S, Calin A. The Bath Ankylosing Spondylitis Radiology Index (BASRI): a new, validated approach to disease assessment. *Arthritis Rheum* 1998;41:2263-70.
13. Creemers MC, Franssen MJ, van’t Hof MA, Gribnau FW, van de Putte LB, van Riel PL. Assessment of outcome in ankylosing spondylitis: an extended radiographic scoring system. *Ann Rheum Dis* 2005;64:127-9.
14. Lubrano E, Marchesoni A, Olivieri I, D’Angelo S, Spadaro A, Parsons WJ, et al. Psoriatic arthritis spondylitis radiology index: a modified index for radiological assessment of axial involvement in psoriatic arthritis. *J Rheumatol* 2009;36:1006-11.
15. Biagioni BJ, Gladman DD, Cook RJ, Eder L, Wakhlu A, Shen H, et al. Reliability of radiographic scoring methods in axial psoriatic arthritis. *Arthritis Care Res* 2014;66:1417-22.
16. Castillo-Gallego C, Aydin SZ, Emery P, McGonagle DG, Marzo-Ortega H. Magnetic resonance imaging assessment of axial psoriatic arthritis: extent of disease relates to HLA-B27. *Arthritis Rheum* 2013;65:2274-8.
17. Nash P, Lubrano E, Cauli A, Taylor W, Olivieri I, Gladman DD. Updated guidelines for the management of axial disease in psoriatic arthritis. *J Rheumatol* 2014;41:2286-9.
18. Lubrano E, Soriano E, FitzGerald O. Can traditional disease-modifying anti-rheumatic drugs be withdrawn or tapered in psoriatic arthritis? *Clin Exp Rheumatol* 2013;31 Suppl 78:S54-8.
19. Salvarani C, Pipitone N, Marchesoni A, Cantini F, Cauli A, Lubrano E, et al. Italian Society for Rheumatology. Recommendations for the use of biologic therapy in the treatment of psoriatic arthritis: update from the Italian Society for Rheumatology. *Clin Exp Rheumatol* 2011;29 Suppl 66:S28-41.
20. Lubrano E, Spadaro A, Marchesoni A, Olivieri I, Scarpa R, D’Angelo S, et al. The effectiveness of a biologic agent on axial manifestations of psoriatic arthritis. A twelve months observational study in a group of patients treated with etanercept. *Clin Exp Rheumatol* 2011;29:80-4.