

Psoriatic Arthritis, Psoriatic Disease, or Psoriatic Syndrome?



Psoriatic arthritis (PsA) is a multifaceted disease. Within this definition, PsA can be recognized by the identification of clinical hallmarks, and generally, rheumatologists diagnose it by the presence of typical skin lesions and articular inflammatory manifestations. This process could be a very easy task especially when some phenotypic manifestations and a detectable objective disease activity are present. Sometimes, the same disease can be very challenging when some manifestations such as pain, fatigue, or even enthesitis are predominant and associated with a less detectable disease activity.

The British physician Verna Wright (1928–1998) is considered the father of the spondyloarthropathies. His interest started with PsA, and then with his junior colleagues, he made a fundamental contribution to this spectrum of diseases¹.

Over the past decade, an increased knowledge of PsA pathogenesis with the identification of various cytokines as targets to be treated has revolutionized the treatment strategy². Therefore, the possibility of personalized medicine, with different phenotypes or biomarkers, has also been proposed³. Hence, there is a potential unmet need to redefine this condition⁴. In fact, we have moved from a simplistic concept of “arthritis” associated with psoriasis to a more comprehensive concept of “disease” because of the frequent association with extraarticular manifestations and comorbidities⁵. In 2006, Scarpa, *et al* proposed a new definition, contemplating PsA as a systemic disease in which, on top of skin and joints, some other characteristics such as extra-articular manifestations and comorbidities should be taken into account⁵. The introduction of this concept has been widely noticed, and the term *psoriatic disease* (PD) is synonymous with PsA. This concept should be regarded as an attempt to explain this disease in a better way. PsA and psoriasis do not always lead to a systemic condition such as PD⁶. Moreover, it still needs to be completely understood whether the pathophysiology of some aspects of PD, such as comorbidities, are always linked depending on the same condition or just simply a coincidence of events, or are they instead related to adverse events of the treatments (e.g., nonsteroidal antiinflammatory drugs)⁶. In fact, the metabolic involvement in the pathogenesis, severity, and progression of PsA remains unclear⁷. Therefore, the concept of PsA as a “syndrome” could be defined as a combination of symptoms

and signs that together represent a disease process⁸. This could be a better solution to describe the phenomena that occur in some patients at different stages of the natural course of PsA. Based on etymology, the term *disease*, from old French *desaise*, means “lack, discomfort;” while the term *syndrome* comes from the Greek and literally means “running together.” In our opinion, the term *psoriatic syndrome* could better describe the phenotypic complexity of PsA. PsA diagnosis is still a clinical one, primarily based on clinical phenotype owing to the various associated features, which can include skin and joint disease. Indeed, PsA, as a syndrome, can develop into different stages of the disease, mainly beginning from a true cutaneous disease that is a dermatological condition that remains so for many years. In fact, it is usually known that only a third of the psoriasis cases develop joint involvement, presenting with some different phenotypes. Moreover, a subclinical joint involvement with synovial inflammation evaluated at imaging in patients with psoriasis but without articular symptoms is well described⁹. Hence, a potential stratification of predominant subsets of the joint disease, the presence of extraarticular manifestations and comorbidities, is necessary for a better treatment strategy. As a consequence of these 2 main domains (skin and joint), the management of these patients is delegated to 2 specialties and aims to achieve remission or low disease activity by treating the main clinical features. To date, the assessment of remission or low disease activity is mainly based on the activity and severity of these 2 domains and on the patient’s perception of disease activity, pain, and quality of life. No importance is placed on other potential characteristics of the disease, such as comorbidities or even extraarticular manifestations¹⁰. So why not try to recognize this as a syndrome?

The idea of this new concept of “taxonomy” is that identification of PsA as a syndrome could be useful for a more personalized medicine strategy. The condition of the potential predominant subsets could be stratified for disease activity, disease severity, and eventually, the presence of extraarticular manifestations and comorbidities. For instance, obesity could be a condition associated with late onset of psoriasis and PsA but not the presence of HLA-B27, possibly identifying a different stage of the disease¹¹.

To understand why it might be useful to adopt the concept

of PsA as a syndrome, we could compare PsA to another disease in rheumatology: systemic lupus erythematosus (SLE). SLE is a prototype of syndrome, a multiorgan disease in which it is possible to recognize different types of SLE (e.g., cutaneous, nephrological, neuropsychiatric, etc.) and in which it is important to identify the various clinical features for a better treatment strategy. In both conditions (PsA and SLE) we have to combine symptoms and signs to identify and to stratify the disease. Interestingly, the 2 conditions could share some potential biomarkers, such as LL37 and anti-LL37, which have recently been proposed as potential biomarkers of PsA¹², suggesting a role in the pathogenesis of this condition. Further, the 2 conditions share pathogenetic pathways and cytokines such as interleukin (IL)-12 and IL-23, as demonstrated by the efficacy in the phase II trial of ustekinumab, a well-known treatment for psoriasis and PsA, in the treatment of SLE¹³.

An explanation of this new concept could be the proposal of PsA pathogenesis in which different sites of onset (skin, joint, entheses, gut) have been recognized and various cells and cytokines have been involved. Therefore, a potential sequence of events can or cannot happen (“run together”) in the same patient and among the patients with PsA¹⁴.

Even if we do agree with the concept of PD, with this new proposal we could have a pathway to follow more strategic disease management, to approach the treatment considering the target to be treated¹⁵ (Table 1), and maybe to learn what more to do about this intriguing and challenging disease.

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Table 1. Targets to be treated for the different features of the disease and consequential potential treatment strategies.

Disease Features	Which Target?	Which Treatment?
Cutaneous involvement	Clear or almost clear skin; PASI75, PASI90, PASI100; BSA < 3%	IL-17 inhibitors IL-12/23 inhibitors Anti-TNF Apremilast MTX Cyclosporine
Enthesitis involvement	No tender and swollen entheses, LEI ≤ 1, pain-VAS ≤ 15, PtGA ≤ 20	Anti-TNF IL-17 inhibitors IL-12/23 inhibitors JAK inhibitors Apremilast ABA
Articular involvement	No tender and swollen joints, DAPSA ≤ 4, ACR50 criteria, BASDAI ≤ 4 (for axial disease), absence of active dactylitis	MTX Anti-TNF IL-17 inhibitors IL-12/23 inhibitors JAK inhibitors Apremilast ABA
Extraarticular involvement (uveitis, IBD)	No uveitis flares, remission according to composite disease activity indices in IBD	MTX SSZ Anti-TNF (monoclonal antibodies) IL-12/23 inhibitors JAK inhibitors
Systemic involvement (systemic inflammation) Comorbidities	Control of systemic inflammation Reduce comorbidities in the future or better control of current comorbidities	Targeting key cytokines and cellular pathways

PASI: Psoriasis Area Severity Index; BSA: body surface area; IL: interleukin; TNF: tumor necrosis factor; LEI: Leeds Enthesitis Index; VAS: visual analog scale; PtGA: patient's global assessment; DAPSA: Disease Activity in Psoriatic Arthritis; ACR50 criteria: American College of Rheumatology 50% criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; IBD: inflammatory bowel disease; MTX: methotrexate; ABA: abatacept; JAK: Janus kinase; SSZ: sulfasalazine.

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