

The Challenge of Early Diagnosis of Psoriatic Arthritis

Early diagnosis is always important in medicine, including in diseases with no effective therapy. Early diagnosis helps avoid unnecessary examinations and elude risky and unhelpful therapies. If an effective therapy is available, the early recognition of the disease allows starting treatment in the early phases of development with the aim of modifying the natural course of the disease.

Early diagnosis is also crucial in a research setting. Studies investigating disease etiology and prognosis are best performed when enrolling patients close to disease onset. In rheumatoid arthritis (RA), early diagnosis and early initiation of aggressive therapy has become a primary objective for clinical rheumatology¹. Studies in the last few decades have shown that an early start of disease-modifying antirheumatic drug (DMARD) treatment can prevent progression of joint damage and functional disability¹.

In the past, in the field of spondyloarthritis (SpA), early diagnosis has not been a priority, especially in the absence of drugs able to modify disease course. The scenario completely changed at the beginning of the new millennium with the introduction of the anti-tumor necrosis factor- α (TNF- α) blocking agents. Today, the early diagnosis of both ankylosing spondylitis (AS) and psoriatic arthritis (PsA) has become a challenging topic^{2,3}.

PsA is classified in the SpA complex together with primary AS, reactive arthritis, arthritis associated with inflammatory bowel disease (IBD), and undifferentiated SpA (uSpA). The clinical spectrum of PsA is wide because of the different targets of the disease, which include the axial skeleton, peripheral joints, peripheral entheses, and the tenosynovial sheaths (i.e., dactylitis), each of which can be involved in isolation. Some years ago, we identified a subset of the disease with isolated peripheral enthesitis and/or dactylitis⁴. In addition, there are forms of PsA lacking skin involvement, since in 20% of cases rheumatologic manifestations antedate the skin lesions of psoriatic disease⁵. If there is a family history of psoriasis, these forms, which often meet classification criteria for uSpA, are designated as PsA sine psoriasis⁵. In the past, PsA was considered a mild disease. In the last 20 years, evidence has accumulated that PsA is erosive and deforming in 40% to 60% of patients

with joint damage that appears in the first years of disease onset⁶⁻¹⁰. Patients with PsA suffer reduced quality of life (QOL) and impairment of functional status and are at greater risk of death compared to the general population^{11,12}. Therapies for PsA were unsatisfactory until some years ago¹³. Traditional DMARD are used in PsA to control the symptomatic manifestations, but there is no evidence that they prevent or significantly decrease rate of progression of structural joint damage. Anti-TNF- α agents have opened new horizons. These drugs reduce the signs and symptoms of inflammation, improve QOL and functional status, and inhibit the progression of structural damage in peripheral joints¹⁴⁻¹⁶. Today, the various sets of recommendations proposed for starting anti-TNF- α blocking agents in PsA state that these drugs should be used only after failure of traditional DMARD^{13,17}. As in RA, such an approach will probably change in the near future, since early intervention should be the most effective clinical strategy in PsA; a pharmacoeconomic study conducted in clinical practice suggests that anti-TNF- α therapy is cost-effective in the first year of treatment (Olivieri, *et al*, unpublished observation).

Classification criteria are available, but there are no diagnostic criteria for PsA. Recently, new classification criteria, the CASPAR (CIASSification criteria for Psoriatic Arthritis), have been developed by experts from 30 rheumatologic centers in 13 countries¹⁸. These criteria have a better specificity and sensitivity than the previously published sets of criteria and should be universally accepted in the next few years. One value of these criteria is that they allow classification of disease, despite the presence of rheumatoid factor and the absence of psoriasis, if the typical findings of PsA are present. Patients without skin lesions should necessarily have a first- or a second-degree relative with psoriasis. A major limitation of the CASPAR criteria is that they may be impossible to apply in recent-onset forms of the disease since they were obtained from a population of patients with long-standing disease (mean disease duration 12.5 yrs). However, a Toronto group have recently studied the performance of the CASPAR criteria at the first visit in 107 consecutive patients with early disease (disease duration <

See Early PsA: The clinical spectrum, page 137

2.5 yrs) and 181 with late disease (> 2.5 yrs)¹⁹. One-hundred six (99.1%) in the first group and 176 (97.2%) in the second met the CASPAR criteria, suggesting that these criteria can also be used to classify patients with early PsA.

Should the CASPAR criteria be used for the diagnosis of early PsA? Classification criteria are proposed with the aim to select patients for clinical studies and for epidemiological purposes. These should not be used for diagnostic purposes. However, in clinical practice, classification criteria are often used for confirming the diagnosis in selected cases. At times, the diagnosis of PsA can also be difficult in cases with late disease²⁰. In early cases, it is even more difficult, as emphasized by studies in patients with early arthritis involving experts²¹. While the CASPAR criteria should be taken into account, a diagnosis should be made even if the criteria are not met. A diagnosis of early PsA should be considered when peripheral arthritis (especially oligoarticular and involving the distal interphalangeal joints), peripheral enthesitis, tenosynovitis, dactylitis, and/or inflammatory spinal pain are present in a patient with psoriasis or a family history of psoriasis. The chronological definition of early PsA, extrapolated from early RA, ranges from 6 to 24 months. In our early PsA clinic, to which dermatologists and general practitioners refer patients with psoriasis and musculoskeletal complaints, we see with increasing frequency patients with PsA that began a few months before (unpublished observation). These patients are interesting for 2 reasons: (1) often they are mono- oligo-symptomatic; and (2) they allow us to understand the exact chronology of the onset of events (i.e., knee synovitis as the first event, dactylitis after 5 days, and heel enthesitis after 15 days). Such data cannot be obtained from patients with disease duration of 1 to 2 years, since they have forgotten the exact time of the events of the early phase of disease development.

In this issue of *The Journal*, Scarpa and co-workers report on the clinical spectrum of early PsA in 47 patients with a disease duration of less than 3 months²². Diagnosis was based on expert judgment. Eighteen patients had the sine psoriasis form of the disease. Three-quarters of the patients had an oligo-enthesoarthritis at clinical examination. Total body scintigraphy and ultrasound revealed a more extensive articular and enthesal involvement than clinically apparent, suggesting the frequent development of mono- and oligoarthritis in polyarthritis observed in several series of patients with PsA. Another important point of this study²² is the confirmation that the structural damage of PsA can be very precocious, as suggested by a previous study²³. Seven patients out of the 47 showed enthesal or articular erosions.

The research agenda of early PsA should address the following topics:

1. Cohort studies of patients with early PsA to better elucidate the evolution of the disease and to identify predictive factors for axial involvement and peripheral enthesitis.

2. Prospective controlled studies assessing the ability of the CASPAR criteria to identify patients with a very short disease duration (< 12 mo). Cases and controls (patients with non-PsA inflammatory joint diseases of similar short duration) should be examined for the criteria at the inclusion visit and at any scheduled followup visits. In cases of poor performance of the CASPAR criteria for early PsA, these studies could identify one or more features allowing the criteria to identify all relevant aspects of early PsA. Similarly, these studies could assess the ability of the criteria to identify patients with a different outcome.

3. Clinical trials aiming to determine whether, in patients with PsA as well as RA, there is a “window of opportunity” for intervention at a stage when tissue injury may still be reversible. These studies should take into consideration the newer agents, but also traditional DMARD, for which there is a lack of evidence of efficacy but no evidence of inefficacy.

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