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EDITORIAL

Nonradiographic axial spondyloarthritis. What brings the new concept?

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It has recently been proposed to introduce a new terminology to identify patients with axial spondyloarthritis earlier: nonradiographic axial spondyloarthritis [1]. This new concept, which does not define a new nosological entity, is the last act, for now, of a long and interesting journey that began in the 1960s and still continues nowadays, fascinating many rheumatologists.

Until the second half of last century, rheumatologists regarded the ankylosing spondylitis or "Morbus Bechterew" as a spinal variant of the rheumatoid arthritis [2]. However, the attentive and careful clinical observation allowed by some rheumatologists among which highlight JM Moll and V Wright intuits that a heterogeneous group of patients with apparently very different diseases shared a lot of clinical aspects and familial aggregation. So, in this way, the concept of the spondyloarthropathies (SpA) was introduced by Moll et al. in 1974 as a family of interrelated disorders sharing clinical and genetic characteristics distinct from rheumatoid arthritis (RA) [3]. At the base of the concept stood the clinical observation of the aggregation of some common diseases (psoriasis, spondylitis, peripheral arthritis, enthesitis, acute anterior uveitis, chronic inflammatory bowel disease) in the same patient or in different members of the same family. One finding that has helped to strengthen the concept of SpA has been, without doubt, its association with HLA-B27, observation made independently but at same time by Brewerton et al. [4] and Schlosstein et al. [5], confirming pathophysiologically the clinical suspicion. Twenty years later, the evidence that a rat transgenic for HLA-B27, spontaneously developed some characteristics of these diseases, provided a definite support for the suspicion long intuited by the pioneers of spondyloarthritis [6].

Presently, it is accepted that the spondyloarthropathies or spondyloarthritis are a heterogeneous group of interrelated rheumatic inflammatory diseases that share common etiopathogenesis, clinical, genetic, and radiological features. SpA encompasses ankylosing spondylitis (AS), reactive arthritis, psoriatic arthritis, inflammatory bowel, and disease-related arthritis, whose estimated prevalence ranges 0.3–0.5 % for AS and 1–2 % of SpA, which is higher than rheumatoid arthritis [7]. These groups of diseases frequently show familial aggregation and are strongly associated with HLA-B27; however, the strength of this association varies markedly between the various types of SpA of which AS remains as the paradigm.

Identification of patients with these diseases has also been a long and interesting road, marked by progress in the deepest knowledge of the clinical expression with new technologies. Initially the patient was identified by appearance: "*Complains of back being "set" for 3 years; cannot turn her head to the side or bend it backwards; is stiff when walking, but is better by day than by night; has pain at lower end of spine and in the hips*" [8]. Radiological findings have been the cornerstone in which the diagnosis has been based, as stated in an early (perhaps the first) serious review by Buckley [9].

Radiographic sacroiliitis has been considered a hallmark of AS and is present in all patients with an established disease, and it is also a requirement for the fulfillment of the modified New York criteria for AS established in 1984, which are widely used as classification and diagnostic criteria in clinical

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practice [10]. The novelty of this set of criteria was the inclusion of inflammatory back pain (IBP) as a clinical criterion replacing the less specific symptom of low back pain that had been used in the Rome and prior New York criteria. The major problem of the modified New York criteria is the reliance on radiographic sacroiliitis as it lacks sensitivity when applied to patients early in their disease course. Furthermore, radiographic sacroiliitis takes several years to develop; thus, the opportunity of an early treatment for the patients by strict application of these criteria is delayed at least 8 years [11] from onset of symptoms and time of diagnosis. The inability of these criteria to identify early forms of the disease led to investigation for other tools, even though the practical rheumatologist already diagnose the disease long before they met the criteria. So, Bernard Amor from Paris proposed a classification criteria based on their own clinical experience and developed according to their own way of assisting patients with spondyloarthritis over many years [12]. These criteria are based on the weighted score of each of the signs and symptoms common to all spondyloarthritis. Simultaneously (a year later) and as a result of a multicenter study, the European Spondyloarthropathy Study Group (ESSG) published their own proposal [13]. The sensitivity and specificity achieved by the Amor and ESSG criteria vary in different series, but these values are usually around 80 and 90 %, respectively. Amor's criteria perform slightly better than ESSG in the classification of early SpA, which may be attributable to the Amor inclusion of response to NSAIDs and HLA-B27 typing [14]. Both set of criteria have been very useful for many years, thanks to their good performances. This was true while the need for early diagnosis was less crucial, when pharmacologic treatment was limited to nonsteroidal antiinflammatory drugs. This has changed with the development of TNF-α inhibitors that are used effectively to treat AS and other SpA in early stages of the disease and the introduction of magnetic resonance imaging (MRI) which can detect early sacroiliitis. The introduction of these developments provided evidence underscoring the shortcomings of these criteria for early recognition (preradiologic) of inflammatory involvement of the sacroiliac joints and the need to develop a new system of classification criteria that overcomes these limitations [15]. In order to accomplish this, it was necessary to redefine some concepts. Assessment of Spondyloarthritis International Society (ASAS) has proposed dividing patients with SpA into two subgroups according to the clinical presentation: predominantly axial SpA and predominantly peripheral SpA (including reactive arthritis, psoriatic arthritis, arthritis associated with chronic inflammatory bowel disease). And it coined the term "preradiographic axial spondyloarthropathy" or "non radiographic axial spondyloarthritis" for patients with clinically predominantly axial disease where no structural damage is detected radiographically on the sacroiliac joints and hence could not be diagnosed with SpA; although clinically indistinguishable, both nonradiographic axial spondyloarthritis and axial SpA represent a unique disease in varying stages. Thus, to improve the classification of axial SpA, MRI of sacroiliitis have been included in the ASAS criteria [16]. Thus, we can apply the ASAS criteria (through the arm image) to patients without radiographic sacroiliitis but positive image (active inflammation/acute) MRI of sacroiliac joints. The new criteria performed well in the validation study. Sensitivity was 82.9 % and specificity was 84.4 %. The new criteria also outperformed the ESSG and Amor criteria, even after incorporating "sacroiliitis on MRI" into the earlier criteria [17].

A substantial proportion of patients with nonradiographic axSpA will develop AS over time but others might have a milder form that will not progress to a full-blown disease. The precise percentage of patients in whom disease progresses is currently unknown.

In summary, this new concept of nonradiographic axial spondyloarthritis represents a step forward in the goal of better and early identification of SpA patients than those previously developed. Probably, the most important contribution of this concept is to lead us to finally confirm (or not) that an effective early therapeutic approach to these patients changes the course of the disease or even induces permanent remission.

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Conflict of interest None.

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