Journal of Autoimmunity 48-49 (2014) 128–133

Contents lists available at ScienceDirect

Journal of Autoimmunity

journal homepage: www.elsevier.com/locate/jautimm

The classification and diagnostic criteria of ankylosing spondylitis

Siba P. Raychaudhuri [a,b,*], Atul Deodhar [c]

[a] VA Sacramento Medical Center, Department of Veterans Affairs, Northern California Health Care System, Mather, CA, USA
[b] Department of Medicine, Division of Rheumatology, Allergy and Clinical Immunology, School of Medicine, University of California, Davis, USA
[c] Division of Arthritis & Rheumatic Diseases (OP09), Oregon Health & Science University, Portland, OR 97239, USA

ARTICLE INFO

Article history:
Received 7 October 2013
Accepted 13 November 2013

Keywords:
Ankylosing spondylitis
Spondyloarthropathy
Diagnosis
Diagnostic criteria

ABSTRACT

Ankylosing spondylitis is the prototype of immune-mediated inflammatory rheumatic diseases grouped under the term spondyloarthritis (SpA). An early diagnosis has now become increasingly important because effective therapies are available and anti-TNF drugs are even more effective if used in early stages of the disease. In ankylosing spondylitis, the 1984 modified New York criteria have been used widely in clinical studies and daily practice but are not applicable in early disease when the characteristic radiographic signs of sacroiliitis are not visible but active sacroiliitis is readily detectable by magnetic resonance imaging (MRI). Thus there has been a need for new classification or diagnostic criteria to identify inflammatory spondyloarthritis at early stage of the disease. This led to the concept of axial SpA to include the entire spectrum of patients with axial disease both, with and without radiographic damage. New classification criteria for the wider group of SpA have been proposed by ASAS (Assessment of Spondylo Arthritis International Society); and the patients are sub-grouped into (1) a predominantly axial disease, termed axial SpA including AS and non-radiographic axial SpA; (2) peripheral SpA. The clinical course and disease process of non-radiographic axial spondyloarthritis remains unclear. However the development of the SpA criteria by ASAS particularly for axial SpA, is an important step for early diagnosis and better management of these patients.

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1. Introduction

The term 'spondyloarthritis' (SpA) designates a group of diseases, which share common clinical and genetic features. These features include involvement of the axial skeleton (sacroiliac joints and spine), peripheral arthritis, enthesitis, dactylitis, acute anterior uveitis, associated psoriasis or inflammatory bowel disease, and presence of the HLA-B27 antigen [1–4]. Depending on the predominant clinical manifestations, SpA can be classified either as axial SpA (characterized by predominant involvement of the spine and/or sacroiliac joints) or as peripheral SpA (peripheral arthritis, enthesitis, and/or dactylitis) [5,6]. Axial SpA is characterized by chronic inflammatory back pain and based on clinical and radiological features can be separated into two groups – (i) ankylosing spondylitis (AS), which is defined by the presence of definite structural changes on radiographs in the sacroiliac joints, and (ii) nonradiographic axial SpA which is defined by the presence of sacroiliac inflammation as detected by MRI or the presence of HLA B27 in combination with the presence of features typical of spondyloarthritis. The spectrum of spondyloarthritis is described in Fig. 1. Ankylosing spondylitis is the prototype of immune-mediated inflammatory rheumatic diseases in the axial spondyloarthritis spectrum.

2. Prevalence of ankylosing spondylitis and spondyloarthritis as a group

Historically, AS was thought to be a disease that almost exclusively affected young men. More recent studies suggest a male-to-female ratio of about 2 or 3 to 1, although there can be considerable geographical and ethnic variation. AS has an estimated prevalence of about 0.5% [7,8] in the Caucasian population, whereas the estimated prevalence of SpA as a group is about 1.5%–2% [7,8]. Human leukocyte antigen (HLA)-B27 is strongly linked to disease susceptibility, and there is a close correlation between the frequency of several subtypes of this allele in a population and the prevalence of AS [4]. In the central European population, the HLA-B27 is as common as 6%–9% [7,9,10]; whereas, in Japanese or Central and South African populations its prevalence is 1% or less with a resulting low AS prevalence [11,12]. However AS can occur in the absence of HLA-B27 and only about 10% of HLA-B27-positive

* Corresponding author. VA Sacramento Medical Center, Department of Veterans Affairs, Northern California Health Care System, 10535 Hospital Way, Mather, CA 95655, USA. Tel.: +1 916 843 7096; fax: +1 916 366 5475.
E-mail address: sraychaudhuri@ucdavis.edu (S.P. Raychaudhuri).

0896-8411/$ – see front matter Published by Elsevier Ltd.
http://dx.doi.org/10.1016/j.jaut.2014.01.015

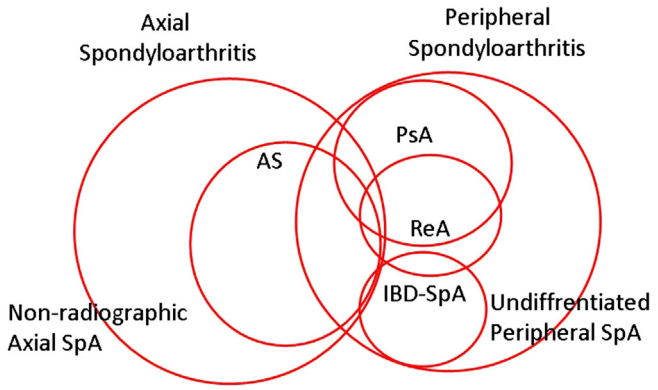

Fig. 1. Venn diagram showing the spectrum of Spondyloarthritis. AS – ankylosing spondylitis. PsA – psoriatic arthritis. ReA – reactive arthritis. IBD-SpA – inflammatory bowel disease associated arthritis.

subjects develop the disease [13], and even HLA-B27-positive identical twins can be discordant for disease incidence as well as severity [14,15].

3. Clinical features

The most characteristic clinical symptom of AS or axial SpA is inflammatory back pain [1,2,16]. The presentation of back pain is not an uncommon occurrence in the general population, making it important to differentiate inflammatory from non-inflammatory causes of back pain. Inflammatory back pain is characterized by stiffness and pain that is worse in the morning or after long periods of inactivity ("gel phenomenon") and is improved with exercise. Patients commonly complain of difficulty sleeping or pain that is not relieved with rest or lying down, or alternating buttock pain [17,18]. Alternating gluteal pain, a more specific feature of inflammatory back pain most likely represents sacroiliac involvement. Sometimes pain and stiffness in the mid-thoracic or the cervical region or chest wall pain may be the initial symptom, rather than the more typical low backache [18]. This may be a relatively more common presentation in women. In addition a major indicative for an inflammatory back pain could be significant pain relief in response to a non-steroidal anti-inflammatory drug (NSAID). The presence of inflammatory back pain alone may not be diagnostic but should trigger suspicion of ax-SpA. In addition certain known associated conditions such as psoriasis, inflammatory bowel disease and uveitis in a patient with inflammatory back may be indicative of ax-SpA. Thus it is important to gather these entire clinical features for an early diagnosis of AS or other forms of ax-SpA.

4. Diagnostic tests: there are no specific laboratory tests for AS or SpA

There are no laboratory findings that are diagnostic of AS. In contrast to other systemic inflammatory diseases such as Lupus and RA, acute phase reactants (erythrocyte sedimentation rate [ESR] and C-reactive protein) may be normal in majority population of SpA patients [19]. Rheumatoid factor and antinuclear antibodies are absent in SpA.

Almost 90% of the patients with AS [20,21] and nearly 70% of the patients with axial SpA [21] are positive for HLA-B27 whereas only 6–10% of the general white population is HLA-B27 positive [20]. This makes this marker relevant as a diagnostic tool. However as mentioned earlier, only a small fraction, about 10% of HLA-B27 positive subjects, develop the disease [13], and even identical twins who are HLA-B27-positive can be discordant for disease incidence as well as severity [14,15]. This clearly indicates that HLA-B27 is neither sufficient nor absolutely necessary for the occurrence of AS. Recently, two new loci related to AS, ERAP1 (ARTS1) and IL23R, have been identified [3]. These facts discourage the use of HLA-B27 as a diagnostic marker for AS or SpA. However HLA-B27 positivity is a key feature in the new ASAS classification criteria for axial-SpA [5,6] hence it is expected this laboratory test will be frequently used for AS and other SpA patients.

5. Diagnosis

In the absence of any diagnostic criteria, the modified New York Classification Criteria are the most widely used tool for the classification of ankylosing spondylitis and they continue to be used for diagnostic purposes too (Table 1) [22]. In most patients, the first symptoms of SpA (usually inflammatory back pain) start in the third or fourth decade of life. As mentioned earlier, inflammatory back is not enough to make the diagnosis; and the diagnosis of AS is based on clinical signs, symptoms along with the radiologic evidences of sacroiliitis. Following evaluations are done to determine the spinal involvement: (i) the modified Schober test is used to measure anterior lumbar spinal flexion (ii) lateral spine motion is assessed using lateral bending of the lumbosacral spine (iii) "Occiput-to-Wall" distance is measured to determine the cervical spine mobility and (iv) chest expansion is measured at the lower end of the xiphisternum to evaluate the rib cage movement. In addition palpation or percussion of the sacroiliac joints may elicit pain, but this does not reliably indicate the presence of sacroiliitis. Placing stress on the sacroiliac joints with the Flexion, Abduction, and External Rotation maneuver and the Gaenslen test can illustrate sacroiliac joint dysfunction and may also produce pain, though the specificity of these tests is not high. Examination and review of the eyes, skin and the cardiovascular and pulmonary systems may uncover extra-articular disease.

Sacroiliitis (Fig 2) is the required and the earliest radiographic manifestation of AS [23]. Thus, pelvic radiographs are essential to make the diagnosis of AS. Radiographic grading of sacroiliitis consists of 5 grades, ranging from 0 = normal to IV = complete ankylosis (Table 2). Due to oblique orientation of the sacroiliac (SI) joints, the standard anteroposterior radiographs of the pelvis may not allow for good visualization of the SI joints. Ferguson view, which is a 30° cephalad angled view of the SI joint may overcome this problem [23]. Isolated SI joint x-rays may result in increased amount of radiation and there is no evidence that this approach is actually superior to the standard pelvic x-ray [24]. Pelvic X-ray also allows to visualize the hip joints which are frequently affected in AS. The classic finding of "squaring" of the vertebral bodies is an important radiological hallmark induced by osteitis and subsequent erosions of the anterior superior and inferior surfaces [25]. Ossification of the spinal ligaments that bridge the intervertebral discs results in the characteristic bony protuberances called

Table 1
Modified New York criteria.

1 Radiological criterion
Bilateral sacroiliitis grade ≥ II or unilateral sacroiliitis grade III to IV
2 Clinical criteria
(a) Low back pain and stiffness of at least 3 months duration improved by exercise and not relieved by rest
(b) Limitation of motion of the lumbar spine in both the sagittal and the frontal planes
(c) Limitation of chest expansion relative to values normal for age and sex
Definite AS is diagnosed if the radiological criterion plus 2 of the 3 clinical criteria are present.