Contents

CHAPTER 2

Clinical Features, Physical Findings, and Diagnosis of Axial Spondyloarthritis

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INTRODUCTION

The term spondyloarthritis (SpA), previously called spondyloarthropathy, defines a group of interrelated chronic inflammatory rheumatic disorders that share several clinical features, as well as genetic predisposing factors, especially *HLA-B*27*, a normal gene that is also present in a small percentage of the general population.[1,2] Its epidemiology is discussed in Chapter 3. The primary underlying pathologic process is enthesitis, defined as inflammation at the sites of bony insertions of tendons and ligaments,[3–5] and associated osteitis and, to a lesser extent, synovitis (see Fig. 2.1). Enthesis is now more broadly defined as "enthesis organ" that also includes the adjacent fibrocartilage, bursa, fat pad, deeper fascia, and trabecular bone because they all function collectively to carry out a common task, namely anchorage and resistance to physical stress.[5,6] Because of the ubiquitous nature of enthesis organs, there is a diversity of resultant clinical manifestations that range from enthesitis, on one hand, to full ankylosis (see Fig. 2.1). The pathogenesis is driven by interaction between a genetically primed host immune system and the gut microbiome, as detailed in Chapters 5 and 6.

As explained further in Chapter 4, SpA patients have now been subclassified, based on their predominant symptoms, into two broad subgroups (see Fig. 2.2):

- A predominantly axial form called "axial SpA" (abbreviated as "axSpA"), best exemplified by patients suffering from ankylosing spondylitis (AS), the prototype of SpA that has afflicted mankind since antiquity. The term AS is a more restrictive form of axSpA that requires X-ray evidence of sacroiliitis.
- A predominantly peripheral form called peripheral SpA (abbreviated as "pSpA") that includes psoriatic arthritis (PsA), enteropathic arthritis (inflammatory arthritis associated with Crohn disease or ulcerative colitis), reactive arthritis, and undifferentiated forms of SpA (abbreviated as "uSpA").

Axial Spondyloarthritis

This book, as its title indicates, deals primarily with axSpA, and the patients suffering from this clinical entity have been further subclassified into two subgroups:

- Patients that show X-ray evidence of sacroiliitis have been termed "radiographic axSpA" (abbreviated as "r-axSpA"), a term that is largely synonymous with AS, as defined by the modified New York criteria.[10] Most of the existing knowledge about axSpA as an entity comes from the long-standing literature primarily based on patients suffering from AS.[1,7–9]
- Patients with "spondylitis disease without radiographic evidence of sacroiliitis,"[11] currently renamed as "nonradiographic axSpA" (abbreviated as "nr-axSpA") (Figs. 2.2 and 2.3). These patients tend to have less pronounced inflammatory signs and predominance of females.[12–15] Not all of them progress to r-axSpA/AS.

This concept of the two subtypes of axSpA has helped in its earlier recognition and treatment, emphasized the wider disease spectrum, and enhanced clinical research.[12–15] It has been proposed that for diagnostic purposes the term axSpA be used, whereas the terms nr-axSpA and AS be used for disease classification and not as separate diagnoses, unless there is a meaningful medical reason to do so.[15]

CLINICAL PRESENTATION

This chapter is based, in part, on the author's earlier publications on this subject.[1,2,7,16–18] The disease symptoms usually start insidiously at young age (late adolescence and early adulthood), ranging from childhood (age 9 years and older) to age 45 years, with the mean age of onset in developed countries hovering around age 23 years. There are rare occurrences of onset of symptoms

Axial Spondyloarthritis. https://doi.org/10.1016/B978-0-323-56800-5.00002-3

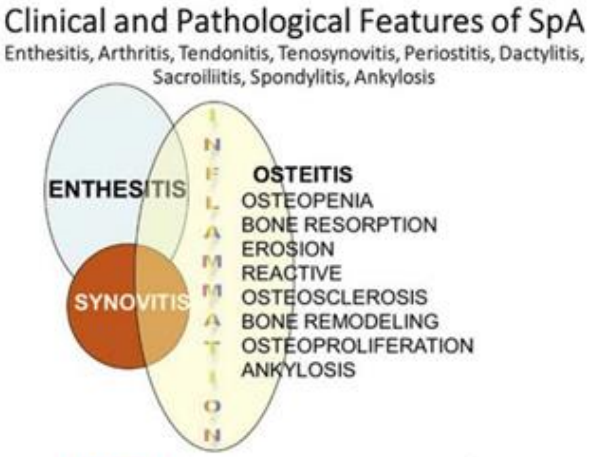

FIG. 2.1 Clinical and pathologic features of SpA.

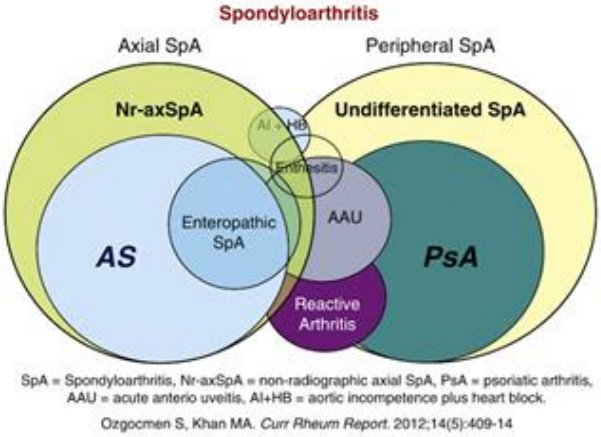

FIG. 2.2 The various forms of SpA have been divided into predominantly axial and predominantly peripheral subgroups. (From Elyan M, Khan MA. Diagnosing ankylosing spondylitis. *J Rheumatol Suppl*. 2006;78:12–23.)

after age 45 years.[19] The patients typically present to their healthcare provider with chronic low back pain and stiffness resulting from inflammation of their sacroiliac joints and/or lumbar spine. However, these symptoms at onset can sometimes be subtle or fleeting.[1,16] Other patients may first present with symptoms resulting from enthesitis, synovitis, and/or involvement of extraskeletal organs, such as the eye, gut, or skin.

Constitutional Symptoms

These include malaise, anorexia, weight loss, or low-grade fever; and they are relatively more commonly observed among patients with more severe disease, childhood onset, and especially in developing countries.[1,7,16] Moreover, fatigue can be a common complaint; it can sometimes be severe and is usually due to active disease and/or inadequate and interrupted sleep as a result of back pain and stiffness.

Axial Pain

The back pain is usually insidious in onset, dull in character, difficult to localize, and initially felt deep in the gluteal region. It can be intermittent and may affect one side or alternate from one side to the other

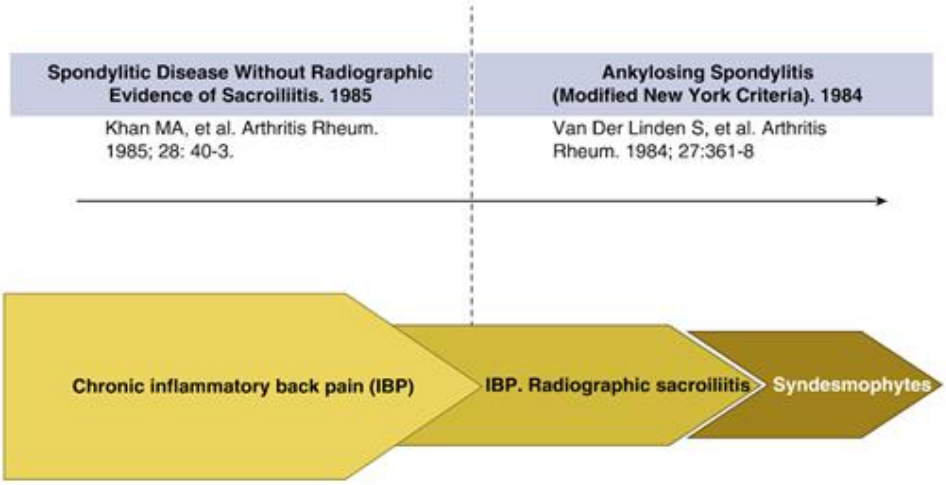

FIG. 2.3 The spectrum of predominantly axSpA: subdivided into "spondylitic disease without radiographic evidence of sacroiliitis," now called nr-axSpA, and r-axSpA that is virtually identical with AS. Not everyone suffering from nr-axSpA progresses to AS, and not every patient with r-axSpA/AS develops syndesmophytes and spinal ankylosis. (Adapted from Khan MA. *Ankylosing Spondylitis—Axial Spondyloarthritis*. West Islip, NY: Professional Communications Inc.(PCI); 2016:1–333.)

in the very early stages before becoming bilateral and/or persistent. Such alternating buttock pain, if present, is a helpful clue in early disease and reflects the fluctuating nature of early inflammation of sacroiliac joints in axSpA.[1,16] Symptoms gradually spread to involve the lumbar spine. Pain and stiffness in thoracic and cervical spine tend to develop later, but they may occasionally be the presenting complaint, especially in women. Tenderness and stiffness of the paraspinal muscles may also be a prominent symptom.

This inflammatory back pain (IBP) has been defined by ASAS criteria as chronic back pain (i.e., duration longer than 3 months) that has at least four of the following five features: an onset before the age of 40 years, insidious onset, improvement with physical activity, no improvement with rest, and night pain that improves upon getting up from bed in the morning and moving about or exercising[20,21] (Table 2.1). It must be kept in mind that among patients with undiagnosed chronic back pain, this definition of IBP does not always mean that an underlying inflammatory condition exists because it has roughly 80%

TABLE 2.1
Features That Suggest Inflammatory Back Pain

Insidious onset	Odds ratio = 12.7
Pain at night (with improvement on getting up)	Odds ratio = 20.4
Age at onset <40 years	Odds ratio = 9.9
Improvement with exercise	Odds ratio = 23.1
No improvement with rest	Odds ratio = 7.7

If at least four out of the above five parameters are met, the criteria had a sensitivity of 77% and specificity of 91.7% in the patients participating in the initial analysis, and 79.6% sensitivity and 72.4% specificity in the validation cohort. Note that these sensitivity and specificity values refer to the presence of IBP, not to the diagnosis of axSpA. Please note that the five parameters are listed in a sequence so that the use of their initial (bold) letter results in a mnemonic IPAIN (or iPAIN to go along with the popular names iPHONE or iPAD) to help recall the five features of inflammatory back pain[107]. The odds ratios of the five parameters are listed to show that pain at night that improves on getting up from bed in the morning and improvement with exercise are the most useful. From Sieper J, et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. *Ann Rheum Dis*. 2009;68(suppl II):ii1–ii44.