Recognition of Preclinical and Early Disease in Axial Spondyloarthritis

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KEYWORDS

• Ankylosing spondylitis • Diagnosis • Magnetic resonance imaging • Genetic testing • Serology

KEY POINTS

- Early diagnosis of axSpA is important because therapy may retard radiographic progression of disease.
- Targeting specific patient groups, such as those with chronic back pain younger than age of 45 years, or extra-articular manifestations of disease may improve timeliness of diagnosis of axSpA.
- Use of genetic and serologic markers may contribute to identification of patients with preclinical or early axSpA.
- The risks and benefits of detection of early or preclinical disease should be considered.

INTRODUCTION

Axial spondyloarthritis (axSpA) is a chronic, inflammatory disease characterized by back pain, spinal ankylosis, peripheral arthritis, and extra-articular manifestations. AxSpA has generally been considered an autoinflammatory disease in the past, because it was thought to lack the autoantibodies that characterize autoimmune rheumatic diseases, such as rheumatoid arthritis and systemic lupus erythematosus. In those conditions, preclinical detection of diagnostic autoantibodies has made very early detection of incipient disease a possibility, although disease does not develop in all those individuals with autoantibodies. Identification of preclinical and early axSpA is therefore a more complex challenge.

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WHY SHOULD AXIAL SPONDYLOARTHRITIS BE DIAGNOSED EARLY?

The estimated prevalence of axSpA is between 0.2% and 1.2% in white European populations.[1] The diagnosis is often delayed by up to 8 years, mainly because sacroiliitis, which is considered a hallmark of ankylosing spondylitis (AS), is not visible on plain radiographs in the early stages of the disease.[2] In recent years, the challenge of early diagnosis of axSpA has become a high priority area of research. Although nonsteroidal anti-inflammatory drugs (NSAIDs) and physiotherapy are the cornerstones of management, tumor necrosis factor inhibitors (TNFi) are effective in patients who are resistant to standard therapy and are more effective in younger patients and those with shorter disease duration.[3–6] It has also been shown that TNFi can suppress the inflammation detected on magnetic resonance imaging (MRI).[7,8] Recent studies have demonstrated that TNFi agents can slow radiographic progression of the disease and the effect is most pronounced when treatment is started earlier in the course of disease.[9] This has added to the imperative for early identification of patients with axSpA.

WHAT IS "EARLY ANKYLOSING SPONDYLITIS"? THE CONCEPT OF AXIAL SPONDYLOARTHRITIS

Historically AS has been defined by the modified New York classification criteria,[10] which require the presence of radiographic sacroiliitis. More recently the use of MRI for earlier detection of inflammation in the sacroiliac joints has led to the identification of patients with features of axSpA who do not fulfill the modified New York criteria, and this has introduced the terminology of nonradiographic axSpA (nr-axSpA). Criteria have been developed for the classification of patients with axSpA including those with nr-axSpA.[11,12] It has been proposed that nr-axSpA may represent an early form of AS. This concept is supported by evidence that some patients do progress to AS over time. Data from early axSpA cohorts have demonstrated that over a 2-year period, approximately 10% of patients with undifferentiated SpA or nr-axSpA progress to radiographic AS.[13–16] However, several patients did not progress to AS over the duration of these studies. This finding, along with the identification of genetic and gender differences between AS and nr-axSpA, has led to the concept of nr-axSpA as a distinct disease entity and not just early AS. A lower frequency of HLA-B27 in nr-axSpA than in AS has been observed in the German Spondyloarthritis Inception Cohort (GESPIC)[16] and in two trials of adalimumab in nr-axSpA, one performed in Germany[3,16] and one an international multicenter trial.[17] In GESPIC the rates of HLA-B27 carriage were 72.6% in nr-axSpA and 84.3% in AS. Gender differences between the two groups have been demonstrated in three German studies with the percentage of males ranging from 31% to 43% in nr-axSpA compared with 65% to 77% in AS.[16,18,19] In general, disease activity and burden of symptoms did not differ, although C-reactive protein levels were lower in nr-axSpA.

EARLY RECOGNITION OF ANKYLOSING SPONDYLITIS IN PRIMARY CARE: THE "BACK PAIN POPULATION"

The first presenting feature in AS is usually low back pain, which is typically characterized by such features as early morning stiffness, relief with exercise, lack of improvement with rest, and nocturnal pain. These constellations of clinical features are key elements of inflammatory back pain (IBP). A description of IBP in association with AS was first published in 1977[20] and several criteria for IBP have been proposed