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Evaluation and Management of the Patient With Suspected Inflammatory Spine Disease

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Abstract

Axial spondyloarthritis (AxSpA) is a chronic inflammatory rheumatic disease characterized by inflammatory back pain (IBP) that manifests in childhood, late adolescence, or early adulthood. Ankylosing spondylitis (AS) and nonradiographic AxSpA represent 2 ends of the AxSpA spectrum. Diagnosis can be challenging because patients develop IBP that may not be associated with radiographic changes in the sacroiliac joints. Patients early in the course of disease are estimated to have at least the same level of disease activity and pain as patients with established disease; thus, they could benefit substantially from earlier diagnosis. Although the recent use of magnetic resonance imaging and its inclusion in diagnostic criteria has enhanced the identification of early AxSpA, improvement in early diagnosis has not been consistently reported across all studies. Limited knowledge of the continuum of AxSpA disease manifestations and lack of recognition of IBP in primary practice may contribute to this. Implementing a referral strategy that identifies patients with IBP for additional testing and assessment may lead to better recognition of early signs and symptoms of AxSpA, thereby offering the potential for improved patient outcomes. This review presents an overview of the epidemiology, clinical characteristics, and burdens of AxSpA, followed by a case presentation outlining approaches to the evaluation and management of a patient with suspected inflammatory spine disease.

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Chronic inflammatory diseases have a detrimental effect on patients because they are associated with pain, impaired function, and diminished health-related quality of life, as well as economic consequences arising from treatment-related costs and a negative effect on employment and participation.[1,2] Spondyloarthritis (SpA) describes a heterogeneous group of chronic inflammatory rheumatic diseases, including ankylosing spondylitis (AS), psoriatic arthritis, enteropathic-related spondylitis, and nonradiographic axial SpA (AxSpA).[3] All of these disorders are associated with familial clustering and human leukocyte antigen B27 positivity (HLA-B27+) in a percentage of patients,[3,4] but differing types of tissue inflammation and structural damage result in a variety of disease phenotypes.[5] Spondyloarthritis can be divided into 2 subgroups—axial and peripheral—according to the predominant location of arthritis.[4] In AxSpA, the main clinical symptom is inflammatory back pain (IBP), and patients have involvement of the sacroiliac joints (SIJ), the spine, or both, whereas patients with peripheral SpA have symptoms predominantly localized to peripheral joints; however, both may occur.[3,4,6] Axial SpA can be further classified as AS or nonradiographic AxSpA.[7] Ankylosing spondylitis is the classic form of the disease[8] and presents with characteristic radiographic damage, and nonradiographic AxSpA presents without radiographic changes but with SIJ inflammation on magnetic resonance imaging (MRI) or computed tomography.[7]

Extra-articular manifestations, including inflammatory bowel disease (IBD), acute anterior uveitis/iritis, aortic insufficiency, and enthesitis, are observed and can substantially affect the prognosis.[9,10] Patients with AxSpA are also at increased risk for cardiovascular and other comorbidities, including ischemic heart disease, hypertension, diabetes mellitus, osteoporosis, and atrioventricular block.[9,11] Note that the hallmark of AS is radiographic detection of sacroiliitis or syndesmophytes on lumbosacral spine radiographs, but MRI

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detection of sacroiliitis may also aid in establishing an accurate diagnosis in patients with AxSpA.[6,12]

Symptoms of AxSpA vary among patients and can change over time, but they typically manifest in late adolescence or early adulthood.[13] Patients experience continuous pain, stiffness, and fatigue if a diagnosis is not established and disease management is not initiated. In addition, AxSpA results in progressive loss of spinal mobility and function without treatment. The prognosis of AxSpA is variable and can be affected by the number of extraspinal manifestations, age at diagnosis, and the treatment received.[14]

EPIDEMIOLOGY OF AxSpA

In the United States, the prevalence of AxSpA is estimated to be 0.7%, with AS and nonradiographic AxSpA each accounting for 0.35% of patients.[15] The prevalence of IBP in US adults aged 20 to 69 years has been estimated to be 5.0% to 6.0%.[16] A significant difference in IBP prevalence by age or sex was not observed, although IBP was more frequent in non-Hispanic white individuals compared with non-Hispanic black individuals. The incidence of AS remained stable from 1980 to 2009 at 3.1 per 100,000 persons, with a male to female ratio of 3.8:1.[10] Notably, findings from this study suggest that long-standing observations of sex-based differences in AS prevalence seem to be declining, as previous publications reported male to female ratios of up to 9:1.[10] Clinical features at presentation and time to diagnosis are generally similar between men and women (time from symptom onset to diagnosis of ~6 years), but uveitis occurs more commonly in women.[10] Furthermore, the prevalence of nonradiographic AxSpA seems to be equal between men and women.[17]

DEMOGRAPHIC CORRELATES

Women with AxSpA may represent an underdiagnosed, undertreated, and understudied population.[18,19] A study of 151 patients (79 men and 72 women) with AxSpA showed that the classic features of AxSpA observed in predominantly male cohorts are often not present in female patients.[20] For example, IBP at disease onset was less common in women compared with men. Although most men and women experienced radiation of low back pain to the buttocks or upper legs, women were significantly more likely to report pelvic, heel, and widespread pain. In addition, enthesopathy was more prevalent in women throughout the disease course, and women with widespread pain had a nearly 2-fold longer delay in time to diagnosis compared with women who did not have widespread pain.[20] Furthermore, disease activity in AxSpA has been longitudinally associated with SIJ inflammation on MRI in men but not in women.[21]

A limited number of studies have been conducted evaluating other demographic correlates in patients with AxSpA. Of note, HLA-B27$^+$ status is associated with younger age at AS onset and diagnosis.[22] In addition, HLA-B27$^+$ is associated with early sacroiliitis and progression to AS in juveniles with SpA, and long-term radiographic progression is more severe in HLA-B27$^+$ men with AS.[23,24]

CHARACTERISTICS OF EARLY DISEASE

The natural history of AxSpA is not well established owing to disease heterogeneity, its slow progression, the previous lack of appropriate outcome measures, and the lack of suitable criteria for early diagnosis.[25] It has not yet been established whether disease progression is linear or whether established disease can be halted.[25] However, the rate of structural progression is low in patients with early nonradiographic AxSpA, and HLA-B27$^+$, smoking, and SIJ inflammation on MRIs at baseline are predictive of disease progression.[26]

Most patients with nonradiographic AxSpA may not develop classic AS, indicating that these are different spectra of the same disease. In a prospective study of 83 individuals with new-onset nonradiographic AxSpA, only 26% of patients progressed to AS over 15 years of follow-up.[27] Based on existing evidence, it is not necessary to differentiate between a diagnosis of nonradiographic AxSpA and AS in clinical practice, and it is more important to distinguish between early and established disease based on duration of symptoms.[7] Furthermore, tumor necrosis factor inhibitor (TNFi) drugs approved for AS are also effective for treating nonradiographic AxSpA.[28-30]

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