

## CLINICAL VIGNETTE

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# Ankylosing Spondylitis in Young Adults: Importance of Early Diagnosis and Treatment

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### *Introduction*

Axial spondyloarthritis (axSpA) is a chronic inflammatory autoimmune disease that affects the spine. AxSpA is classified into two subtypes, ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA). The former, AS, has radiographic evidence of disease, whereas the latter, nr-axSpA, does not. Studies report 11.6% of patients with nr-axSpA will develop AS within 2 years,<sup>1</sup> and 26% of patients with nr-axSpA will develop AS within 15 years.<sup>2</sup> Symptoms typically present before age 30,<sup>3</sup> with average age of diagnosis in AS being > 33.<sup>4</sup>

AS causes chronic pain and stiffness of the spine, neck, and hips, which worsens after periods of inactivity and improves with movement or exercise. In more advanced stages, AS causes ankylosis fusion of the spine, or spinal fusion, resulting in limited range of motion and decreased flexibility of the spine, characterized by hunched posture. The inflammatory processes of AS are primarily axial, but common extra-articular manifestations include anterior uveitis, psoriasis, or colitis.

There is a lack of understanding about the pathogenesis of AS and the progression from nr-axSpA to AS. However, there is a strong correlation between AS and heritability. The most widely understood risk factor for AS is the major histocompatibility complex (MHC) class I allele human leukocyte antigen (HLA) B27, with 90-95% of people with AS carrying this gene.<sup>5</sup> However, not everyone with this gene variant will develop AS. Approximately 5-6% of the US population carry this gene,<sup>6</sup> while the prevalence of AS is much lower, affecting approximately 0.2% to 0.5% of the US population.<sup>7</sup>

Additional objective findings used to support the diagnosis of AS include radiographic evidence of disease (inflammation, sacroiliitis, intra-articular findings), and elevated inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). AS is considered seronegative, as serologies commonly used to diagnose seropositive autoimmune diseases (i.e., rheumatoid arthritis, lupus) are not present.

Pharmacological treatments for AS include nonsteroidal anti-inflammatory drugs (NSAIDs) and biologics such as TNF- $\alpha$  inhibitors (TNFi). Additional treatments include methotrexate and sulfasalazine, although these have shown to be less efficacious in treating primarily axial involvement.<sup>8,9</sup>

### *Case Report*

A 22-year-old male who recently relocated from Belize presented to rheumatology with hip, back, and neck pain and a personal medical history of total left hip replacement.

The patient reported that his hip pain began at the age of 14, becoming more severe around age 17. At the age of 21, while visiting a relative in New York, the patient presented to a local ER with severe left hip pain and subsequently underwent a left total hip replacement.

Plain radiographs of the cervical spine, lumbar spine, and right hip were taken during hospitalization, which were notable for fusion of the facets, a bridging osteophyte at C3-C4 and sclerotic lucent osseous lesion of the right femur with degenerative changes of the right hip. Radiographs of the lumbar spine were unremarkable. Inflammatory markers, including CRP and ESR, were elevated. The patient was instructed to follow up with a rheumatologist postoperatively, however, his appointment in New York was canceled and he returned to Belize. He explained that there is a shortage of physicians in Belize with no practicing rheumatologists, so he had not seen a physician since his surgery.

Physical exam at rheumatology was remarkable for limited range of motion in the cervical spine with less than 10-20 degrees on lateral rotation. Tragus to wall distance was 17 cm (with under 10 cm being normal), and occiput to wall distance was 8 cm (with 0 cm being normal). The patient had a severe limp and very limited range of motion in the right hip. His review of systems was otherwise negative for peripheral joint pain, eye pain, psoriasis, or family history of autoimmune disease.

Serologies were negative for antinuclear antibody (ANA), anti-double stranded DNA antibodies (anti-dsDNA), rheumatoid factor (RF), cyclic citrullinated peptide (CCP) antibody. Laboratory testing was notable for elevated ESR at 33 mm/hr., elevated CRP at 105 mg/L, and HLA-B27 positive. Plain radiographs of the cervical spine showed diffuse bony ankylosis with possible scleritis in the right sacroiliac joint.

A diagnosis of HLA-B27 positive Ankylosing Spondylitis was established and he was started on weekly injections of the TNFi etanercept. If the patient regains enough flexibility in the neck

to pass his driver's test, we intend to proceed with infliximab infusions.

### Discussion

This case illustrates the critical nature of early intervention in AS, as the patient's aggressive disease progressed to ankylosis of the cervical spine prior to the average age of symptom onset. Interestingly, in a study by the Royal National Hospital for Rheumatic Diseases on age of onset and disease expression in AS, researchers reported an increase in the prevalence of total hip replacements in early-onset AS compared to late-onset AS, approximately 18% and 8%, respectively.<sup>10</sup> However, age of onset had no significant effect on radiographic progression across the same cohort.<sup>10</sup> Further research may provide a deeper understanding of factors that contribute to more aggressive disease progression as highlighted in this case.

### Conclusion

Given the complicated nature and inconclusive pathogenesis of such cases, seronegative patients face a greater risk of misdiagnosis or delayed diagnosis, resulting in irreversible, potentially physically deforming and disabling—disease progression before treatment is initiated. This is especially true in cases where symptoms present before radiologic progression is detected. Scientific advances have the potential to innovate and simplify the diagnostic criteria and evaluation for primary care clinicians, especially in medically underserved areas lacking availability of sub-specialists.

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