Axial spondyloarthritis: diagnosis and management

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Primary care plays a vital role in the identification and early referral of axial spondyloarthritis. Here, the authors discuss how to recognise the signs and recommend a multidisciplinary approach to management.

Axial spondyloarthritis (AxSpA) is a chronic inflammatory disorder of which ankylosing spondylitis (AS) is the most recognisable phenotype. AxSpA typically affects young individuals and may remain undiagnosed for decades due to the paucity of specific signs and symptoms associated with the disease. The cardinal symptom of AxSpA and AS is inflammatory back pain (IBP), that can sometimes be indistinguishable from chronic back pain of other cause.

Background

AS is a common inflammatory condition of the axial skeleton with an estimated prevalence of 0.86 per cent among whites. The name AS is derived from the Greek word ankylosis meaning bent or crooked; and spondyls meaning vertebrae. Indeed this came from the observation of extreme back deformities stemming from the structural involvement characteristic of late disease. The current diagnostic criteria, the modified New York criteria, are heavily hinged on the presence of unequivocal radiographic changes of bone damage in the sacroiliac joints. These bone changes, namely sclerosis, erosions, new bone formation and/or ankylosis, may not be readily visible in the early disease stages, hence making it impossible for the diagnosis of AS to be made based on conventional radiography appearances. Typically, these radiographic changes only show after 10–15 years of disease activity and in some cases may never appear yet the patient may suffer greatly. The advent of MRI as a sensitive imaging tool, has allowed for a greater insight into the pathogenesis of AxSpA, helping to identify inflammatory spinal disease up to a decade earlier than conventional radiography. This stage of disease is known as non-radiographic (nr-AxSpA) because of the lack of radiographically identifiable features. In an attempt to address this large group of patients, new nomenclature was recently introduced by the Assessment in Spondyloarthritis Society (ASAS).

AxSpA is one of the clinical entities included in the clinical family of spondyloarthritis, that also includes psoriatic arthritis, reactive arthritis and arthritis associated to inflammatory bowel disease. Some of these entities may affect...
primarily the peripheral rather than the axial skeleton although they share many common articular and extra-articular features (see Figure 1).

This article will focus on AxSpA of which two large subgroups are recognised: non-radiographic (nr-AxSpA) and radiographic (AS) (see Figure 1), with the latter being one possible clinical ‘outcome’ of any of the clinical entities known as spondyloarthropathies.

Aetiology and epidemiology
Most of the published epidemiological data stem from AS cohorts showing a higher male prevalence of this subgroup (male to female ratio of 2:1) with patients typically presenting within the third decade of life with less than 5 per cent presenting above age 45.5

The cause of AS is unknown, although there is a strong genetic component with approximately 90 per cent of AS patients carrying the HLA-B27 gene.6 It is also likely that many other genes around the MHC and complex environmental factors play a role.

Understanding of how nr-AxSpA interrelates with AS is still unclear. In the absence of longitudinal inception cohorts, data derived from cross-sectional interventional trials show that these patients differ from the AS group with a predominant female population and less spinal inflammation. This is consistent with previous findings that male AS patients have worse radiological outcomes.7

It remains unclear what proportion of nr-AxSpA patients will evolve into AS however, both groups appear to have a similar burden of disease that impacts significantly in the quality of life of individuals with most of the loss of function occurring within the first 10 years of disease in AS.3,8

Presenting features and co-morbidities
Identifying patients with AxSpA early can be difficult because of the lack of pathognomonic signs and symptoms. Indeed, one of the cardinal features of AxSpA is IBP, that can be difficult to differentiate from chronic pain of non-inflammatory origin. There are many clinical criteria to identify IBP (see Figure 2),9 the latest of which has been incorporated into the new classification criteria for AxSpA.4

Aside from IBP, inflammation within the sacroiliac joints can cause alternating buttock pain whereas inflammation within sterno-costal joints can cause anterior chest wall pain. Inflammation may also occur at any site of ligament, tendon, joint capsule or fascia insertion into bone; known as entheses. These enthesitis are most commonly seen at the Achilles tendon or plantar fascia.10 Other peripheral musculoskeletal features include peripheral arthritis and dactylitis (sausage digits) where inflammation arises within the flexor tendon, sheath and adjacent soft tissue causing the entire digit to swell.

Non-musculoskeletal associations seen in AxSpA include psoriasis, inflammatory bowel disease, aortitis, pulmonary fibrosis and uveitis, that can represent an ophthalmology emergency in some cases as permanent visual damage may occur.

Young patients with AS are at higher risk of cardiovascular disease and stroke in comparison to healthy controls and it is likely that this is partly due to chronic inflammation and chronic usage of anti-inflammatory drugs.11,12 Patients should benefit from early cardiovascular risk assessments and monitoring. Smokers should be encouraged to quit as this is an independent risk factor for severe disease, poor function and health.13 Finally, long-term inflammation can cause osteopenia and osteoporosis in up to 40 per cent of AS patients aged over 50 years and patients should be advised to have a diet rich in calcium and vitamin D.14

### ASAS criteria for inflammatory back pain (IBP)

<table>
<thead>
<tr>
<th>Must have back pain for &gt;3 months</th>
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<td>Patients must answer yes to 4 out of the 5 following criteria</td>
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<td>1. improvement with exercise</td>
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<tr>
<td>2. pain at night (with improvement on getting up)</td>
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<td>3. insidious onset</td>
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<td>4. age at onset of less than 40 years</td>
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<td>5. no improvement with rest</td>
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Figure 2. ASAS criteria for IBP (sensitivity of 79.6 per cent and specificity of 72.4 per cent in the validation cohort)9
Diagnosis and classification

In a patient with suspected AxSpA, a referral to rheumatology should be initiated as early as possible. Aside from a comprehensive clinical history, patients may require a plain AP pelvic film to visualise the sacroiliac joints and to allow for assessment of hip joints, that can be affected early in poor prognosis cases. If no diagnostic abnormalities are elucidated in these films, MRI of the sacroiliiac joints and spine may be useful to identify inflammatory lesions suggestive of an active disease state. These imaging tests should only be requested and interpreted by experts trained in the recognition of AxSpA. Blood tests include HLA-B27 and CRP.

In a patient with clinical history suggestive of AxSpA, the diagnosis may be aided by the ASAS criteria (see Figure 3). If patients fulfil these criteria but do not yet have X-ray changes of sacroilitis they are labelled as nr-AxSpA. If they do have X-ray changes, and fulfill the modified New York criteria, they may be diagnosed as established AS (see Figure 4).

Management

Management of AxSpA should be undertaken as part of a multidisciplinary approach inclusive of education, exercise, medication and psycho-social support. Patients should be advised to keep active and ideally should receive an initial physiotherapy assessment with the opportunity to participate in individual or group therapy sessions. Video demonstrations of exercises aimed at patients with AS are available through the National Ankylosing Spondylitis Society (NASS). Furthermore, NASS provides a wealth of information and a support network on their website (www.nass.co.uk).

First line medications

Current NICE guidelines state patients should be initially trialed on non-steroidal anti-inflammatory (NSAID) therapy or COX-2 inhibitors as 70–80 per cent of patients will show good response. The European League Against Rheumatism (EULAR) recommends continuous use of anti-inflammatory agents in patients with persistant, active disease although their use in inactive disease is also supported by preliminary data showing slower radiological progression in the spine.

This however needs to be balanced against the potential risk for side-effects in particular gastrointestinal and cardiovascular, the latter already increased in this group when compared to a healthy population.

Corticosteroids given intra-articularly into peripheral joints or sacroiliac joints can be very effective, however benefits tend to be short term. IV or IM corticosteroids are sometimes used although there is a lack of evidence to support their efficacy.

Second line medications

Unlike other inflammatory arthritides, there are no trials supporting the use of traditional disease-modifying anti-rheumatic drugs (DMARD) in axial disease. The only therapeutic agents proven to be efficacious in all stages of AxSpA are the biologics, in particular the inhibitors of the pro-inflammatory cytokine TNF-alpha inhibitor (TNFi).

Currently in the UK, NICE guidance supports the use of anti-TNF medications; adalimumab, etanercept and golimumab in AS. In the ATLAS study, 58.2 per cent of patients receiving adalimumab achieved at least a 20 per cent improvement (ASAS 20) at week 12, with similar numbers seen in other trials for etanercept and golimumab. Other promising drugs include the anti-IL-17 inhibitor secukinumab currently undergoing phase III trials.

ASAS criteria for axial spondyloarthritis

- ≥1 clinical criteria
- OR
- HLA-B27 plus ≥2 other SpA features

Figure 3. ASAS criteria for axial spondyloarthritis

SpA features

- inflammatory back pain (IBP)
- arthritis
- enthesitis (heel)
- uveitis
- dactylitis
- psoriasis
- Crohn’s/colitis
- good response to NSAIDs
- family history for SpA
- HLA-B27
- elevated CRP

Figure 4. Modified New York criteria (1984)

Modified New York criteria (1984)

- ≥1 clinical criteria
- AND
- ≥1 radiological criteria

- low back pain and stiffness for >3 months, improves with exercise but not with rest
- limitation of lumbar spine in sagittal and frontal planes
- limitation of chest expansion relative to normal values
- radiographic sacroiliitis grade ≥2 bilaterally
- radiographic sacroiliitis grade ≥3 unilaterally

Figure 4. Modified New York criteria (1984)
The role of primary care in AxSpA is of utmost importance to:

- identify patients with IBP and refer to rheumatology early
- provide life long support including psycho-social and physical therapy. Patients should maintain postre and participate in exercise
- provide early cardiovascular risk assessment and advise smoking cessation
- encourage adequate calcium and vitamin D intake or replacement if bone loss is already present.

NICE recommendation on biologic use in these patients is currently under review. It is expected that the updated version would support the use of TNFi across the clinical AxSpA spectrum as current guidelines only refer to AS. Indeed, the need for use of these drugs in the non-radiographic stage (nr-AxSpA) is currently unmet despite increasing evidence of enhanced response in the earlier disease stages. There is also some preliminary data suggesting a positive effect of bisphosphonates (pamidronate and zoledronic acid) in the treatment of symptoms and inflammatory markers in active AS, although the mechanisms behind this response are not clearly elucidated.

References

Declaration of interests
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