

Early diagnosis crucial in ankylosing spondylitis

Malaviya AP, Ostor AJK. Early diagnosis crucial in ankylosing spondylitis.
Practitioner 2011; 255 (1746):21-24

Dr Anshuman P Malaviya MBBS MD MRCP
Rheumatology Clinical Research Fellow

Dr Andrew JK Ostor MA MBBS FRACP
Director, Rheumatology Research Unit and Consultant Rheumatologist
Rheumatology Clinical Research Unit, Addenbrooke's Hospital, Cambridge



Practitioner
Medical Publishing Ltd

Early diagnosis crucial in ankylosing spondylitis

AUTHORS

Dr Anshuman P Malaviya

MBBS MD MRCP
Rheumatology Clinical
Research Fellow

Dr Andrew JK Ostor

MA MBBS FRACP
Director, Rheumatology
Research Unit and
Consultant Rheumatologist

Rheumatology Clinical
Research Unit,
Addenbrooke's Hospital,
Cambridge

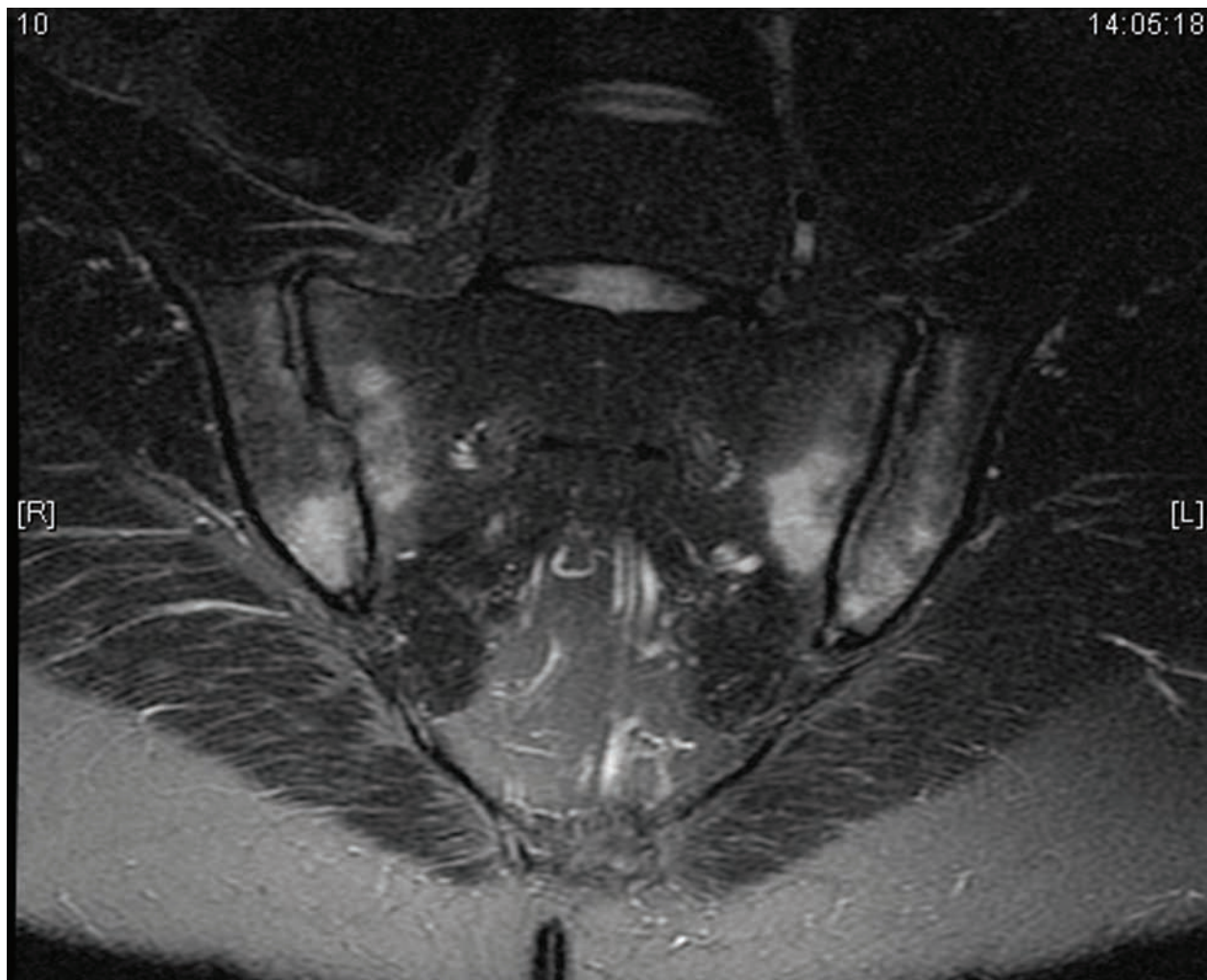


FIGURE 1

MRI scan showing bilateral sacroiliitis: MRI helps identify patients with ankylosing spondylitis early in the course of the disease

Why is early diagnosis so important?



BACK PAIN IS COMMON WITH UP TO 9% OF THE POPULATION CONSULTING THEIR GP

with this problem each year.¹

As the vast majority of these patients have non-specific back pain, it is often difficult to identify those with inflammatory disease such as ankylosing spondylitis (AS). It is critical to make this distinction as AS, if untreated, may cause significant morbidity with a substantial

How should diagnosis be confirmed?

socio-economic impact both on the individual and society. Early diagnosis is particularly important as newer therapies are able to contain this condition and even induce remission in some cases.

AS is an inflammatory autoimmune disorder that predominantly affects the spine. It is one of a group of conditions called inflammatory spondyloarthropathies, see table 1, p22. AS affects about 0.2-0.5% of the population.²

It is at least twice as common in men

What are the evidence-based treatment options?

than women and most often manifests in the third to fifth decades. It is estimated that up to 5% of patients with chronic lower back pain in primary care have inflammatory disease.³ Diagnosis is usually delayed at least partly through lack of awareness of this condition.⁴

PATHOGENESIS

The association between AS and HLA-B27 is the strongest known association between a disease

SYMPOSIUM MUSCULOSKELETAL MEDICINE

ANKYLOSING SPONDYLITIS

Table 1

The spondyloarthropathies (SpA) seen in association with HLA-B27⁵

Condition	Proportion of patients with HLA-B27
Ankylosing spondylitis	90-95%
Psoriatic SpA	50-60%
Enteropathic SpA (SpA associated with inflammatory bowel disease)	50-60%
Reactive arthritis	60-90%
Undifferentiated SpA	unclear
Juvenile SpA	80-90%
Isolated peripheral enthesitis	unclear

and a major histocompatibility complex antigen. The prevalence of HLA-B27 varies vastly between different ethnicities and is estimated to be 8% in the general population in the UK.⁵ Although only 1% of patients with HLA-B27 develop AS, 90-95% of patients with AS are positive for HLA-B27. Various hypotheses have been proposed to explain the pathogenetic role of HLA-B27 although its exact role remains unclear. Immune dysfunction is the hallmark of this condition and it may be triggered by infection.⁵

The primary site of inflammation in AS is the entheses, the sites of insertion of tendons and ligaments into bone.

Tumour necrosis factor (TNF) and other cytokines play a role in perpetuating the inflammatory process. If the inflammation remains untreated, there is resultant fibrosis and ultimately ossification at the enthesal sites, so-called bamboo spine which is now infrequently seen.

DIAGNOSIS

AS should be suspected in patients who report back pain and stiffness with rest, especially in the morning, which improves with exercise. Although the condition affects both the sacroiliac joints, a proportion of patients report pain radiating into the buttocks which may be unilateral or alternate, particularly in the early stages.

In addition to the spine, large joint synovitis may develop as well as features of enthesal involvement (such as tennis/golfer's elbow, Achilles tendinitis and plantar fasciitis).

Symptoms are usually associated with a modest elevation of inflammatory markers (ESR/CRP). Pelvic radiographs may reveal sacroiliitis, although MRI is a more sensitive tool, particularly in early disease.

The 1984 modified New York criteria formed the mainstay for the diagnosis of AS for several decades and required evidence of sacroiliitis on plain

Table 2

Assessment of Ankylosing Spondylitis International Society (ASAS) criteria for classification of axial spondyloarthritis⁶

In patients with chronic back pain and age at onset of pain <45 years axial spondyloarthritis can be diagnosed by:

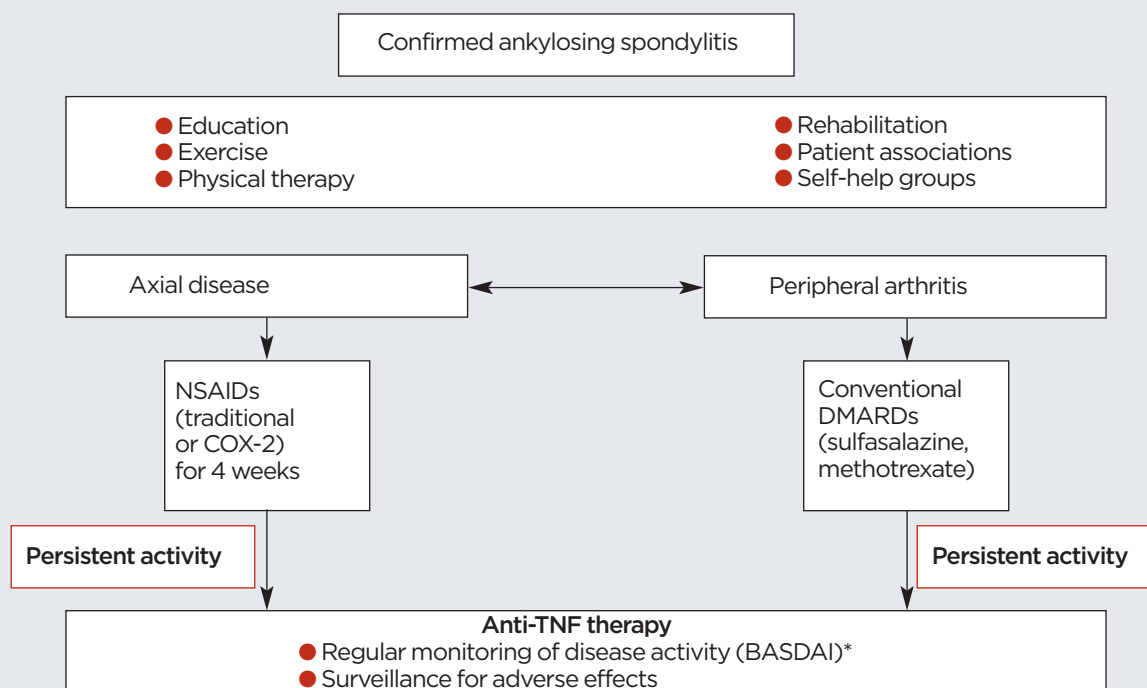
Sacroiliitis on imaging (active inflammation on MRI highly suggestive of SpA; definite radiographic evidence of sacroiliitis according to modified New York criteria) plus ≥ 1 SpA feature or HLA-B27 plus ≥ 2 other SpA features

SpA features

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

Figure 2

Simplified treatment algorithm for ankylosing spondylitis



*BASDAI (Bath AS disease activity score) is a well validated disease activity score that is widely used in clinical practice and in research to monitor disease activity

key points

SELECTED BY

Dr Peter Saul

GP, Wrexham and associate GP Dean for North Wales

Ankylosing spondylitis (AS) is an inflammatory autoimmune disorder that predominantly affects the spine. If untreated it may cause significant morbidity. Early diagnosis is particularly important as newer therapies are able to contain this condition and even induce remission.

AS affects about 0.2-0.5% of the population. It is at least twice as common in men than women and most often manifests in the third to fifth decades. It is estimated that up to 5% of patients with chronic lower back pain in primary care have inflammatory disease. Although only 1% of patients with HLA-B27 develop AS, 90-95% of patients with AS are positive for HLA-B27. Immune dysfunction is the hallmark of this condition and it may be triggered by infection. The primary site of inflammation in AS is the entheses, the sites of insertion of tendons and ligaments into bone. If the inflammation remains untreated, there is resultant fibrosis and ultimately ossification at the enthesal sites.

AS should be suspected in patients who report back pain and stiffness with rest, especially in the morning, which improves with exercise. Although the condition affects both the sacroiliac joints, a proportion of patients report pain radiating into the buttocks which may be unilateral or alternate, particularly in the early stages. In addition to the spine, large joint synovitis may develop as well as features of enthesal involvement. New classification criteria take into account early sacroiliitis evident on MRI scan and allow a diagnosis to be made far earlier than was previously possible.

A proportion of patients respond well to NSAIDs coupled with a structured physiotherapy and exercise programme. However, about half these patients need escalation to biologic therapy. It is recommended that patients take the lowest dose of an NSAID with the best safety profile to control symptoms. Patients with a suspected diagnosis should be referred to secondary care in order to confirm the diagnosis and commence treatment.

Conventional DMARDs such as methotrexate and sulfasalazine have no role in the treatment of axial spondyloarthritis and enthesopathy. Biologic therapy has revolutionised the management of AS with four drugs currently licensed for treatment: infliximab, etanercept, adalimumab and golimumab. These drugs bind to, and eliminate, TNF. Although there is significant improvement in clinical outcomes and quality of life indices, the evidence to support radiological non-progression is limited and up to 20-40% of patients do not respond to anti-TNFs.

radiographs and at least one of the following three criteria to be met:

- low back pain and stiffness for more than three months which improves with exercise but is not relieved by rest
- restriction in lumbar movements in both plains
- limitation of chest expansion

These diagnostic criteria are somewhat obsolete and have been replaced by new classification criteria that take into account early sacroiliitis evident on MRI scan, see table 2, opposite. Figure 1 on p21 shows the appearance of sacroiliitis on MRI scan.

‘AS should be suspected in patients who report back pain and stiffness with rest, especially in the morning, which improves with exercise’

MANAGEMENT

A simplified algorithm for the treatment of AS is shown in figure 2, opposite. A proportion of patients respond well to NSAIDs coupled with a structured physiotherapy and exercise programme. However, about half these patients need escalation to biologic therapy.⁶

We recommend that patients with a suspected diagnosis be referred to secondary care in order to confirm the diagnosis and commence treatment.

NSAIDs and physiotherapy

NSAIDs form the mainstay of treatment of patients with AS. There is often a dramatic improvement in symptoms; however, it would appear that these drugs do not alter the natural course of the disease. In addition to gastrointestinal side effects, there is evidence to support adverse cardiovascular risk with long-term use. It is therefore recommended that patients take the lowest dose of an NSAID with the best safety profile to control symptoms. COX-2 inhibitors have been found to be effective in AS and are often used in patients as alternatives; albeit sparingly.

A recent Cochrane systematic review suggested that physiotherapy and

exercise therapy was beneficial in AS.⁷ It concluded that home-based exercise therapy was better than no therapy; that group physiotherapy was superior to home-based therapy and that inpatient physiotherapy followed by group therapy was the best. It is, however, not clear which patients are most likely to benefit from these interventions.

DMARDs and corticosteroids

Conventional DMARDs such as methotrexate and sulfasalazine have no role in the treatment of axial spondyloarthritis and enthesopathy. There is some evidence of efficacy in peripheral arthritis; and they should be reserved for this indication.

Corticosteroids are also less efficacious in AS than in rheumatoid arthritis and are seldom used to treat acute flares.

Biologic therapy

Biologic therapy has revolutionised the management of AS with four drugs currently licensed for treatment: infliximab, etanercept, adalimumab and golimumab. These drugs bind to, and eliminate, TNF and are highly efficacious in AS. Numerous large randomised controlled trials have demonstrated their efficacy and safety in AS.^{8,9} NICE has approved the use of these drugs for patients with active disease who have failed a trial of two NSAIDs.^{10,11} There is evidence to suggest that this cohort of patients is most likely to progress if left untreated.

Although there is significant improvement in clinical outcomes and quality of life indices, the evidence to support radiological non-progression is limited.¹² Furthermore, up to 20-40% of patients do not respond to anti-TNFs.¹² As a result there continues to be an unmet need and a wide range of novel biologics therefore are being trialled in AS to try to fill the void.

‘Early diagnosis and therapy may reduce the impact of this condition’

CONCLUSION

AS with its striking clinical features is likely to be encountered by primary care physicians. The role of the GP in

»

SYMPOSIUM

ANKYLOSING SPONDYLITIS

identifying AS is critical. This requires skill in sifting inflammatory disease from the sea of patients who present with back pain. Early diagnosis and therapy may reduce the impact of this condition on the individual and also help save healthcare costs in the long term.

We would strongly recommend referral of suspected cases to the local rheumatology service. MRI helps identify patients early in the course of the disease and current management strategies, including anti-TNFs, are very effective at reducing symptoms and improving quality of life. However, despite all the recent advances, anti-inflammatory drugs, patient education and physiotherapy remain the cornerstone of therapy.

REFERENCES

- 1 World Health Organization. The burden of musculoskeletal conditions at the start of the new millennium. *World Health Organ Tech Rep Ser* 2003; 919:1-218
- 2 Reveille JD. Epidemiology of spondyloarthritis in North America. *Am J Med Sci* 2011;341(4):284-6
- 3 O'Shea FD, Boyle E, Salonen DC et al. Inflammatory and degenerative sacroiliac joint disease in a primary back pain cohort. *Arthritis Care Res (Hoboken)* 2010;62:447-54
- 4 Hamilton L, Gilbert A, Skerrett J et al. Services for people with ankylosing spondylitis in the UK - a survey of rheumatologists and patients. *Rheumatology* 2011;50(11):1991-8
- 5 Sheehan NJ. The ramifications of HLA-B27. *J R Soc Med* 2004;97(1):10-14
- 6 Sieper J, Rudwaleit M, Baraliakos X et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis (Supplement). *Ann Rheum Dis* 2009;68:ii1-ii44
- 7 Dagfinrud H, Kvien TK, Hagen KB. Physiotherapy interventions for ankylosing spondylitis. *Cochrane Database Syst Rev* 2008;1:CD002822
- 8 Baraliakos X, Listing J, Fritz C et al. Persistent clinical efficacy and safety of infliximab in ankylosing spondylitis after 8 years- early clinical response predicts long-term outcome. *Rheumatology* 2011;50(9):1690-9
- 9 Braun J, van der Horst-Bruinsma IE, Huang F et al. Clinical efficacy and safety of etanercept versus sulfasalazine in patients with ankylosing spondylitis: a randomized, double-blind trial. *Arthritis Rheum* 2011;63(6):1543-51
- 10 National Institute for Health and Clinical Excellence. TA143. Adalimumab, etanercept and infliximab for ankylosing spondylitis. NICE. London. 2008
- 11 National Institute for Health and Clinical Excellence. TA233. Golimumab for the treatment of ankylosing spondylitis. NICE. London. 2011
- 12 Dougados M, Baeten D. Spondyloarthritis. *Lancet* 2011;377(9783): 2127-37

Useful information

National Ankylosing Spondylitis Society (NASS)

NASS is an independent charity that provides information for patients, their families and healthcare professionals.
www.nass.co.uk

We welcome your feedback

If you would like to comment on this article or have a question for the authors, write to:
editor@thepractitioner.co.uk