

Early recognition pivotal in the management of spondyloarthritis

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FIGURE 1

X-ray of a 34-year-old man with a diagnosis of HLA-B27 positive ankylosing spondylitis and fusion of both sacroiliac joints

What are the different types of spondyloarthritis?



SPONDYLOARTHRITIS IS A DIVERSE GROUP OF INFLAMMATORY MUSCULOSKELETAL

diseases that can present as axial and/or peripheral disease. There is a well established association with human leukocyte antigen HLA-B27.

The spondyloarthritis group is divided into two main subgroups: axial spondyloarthritis and peripheral spondyloarthritis. These may exist as separate entities or may coexist in the same patient.

Axial spondyloarthritis can be further subdivided into non-radiographic axial spondyloarthritis¹ and ankylosing

What are the evidence-based treatments?

spondylitis, where the first subgroup does not necessarily have a natural progression towards ankylosing spondylitis. Peripheral spondyloarthritis encompasses psoriatic arthritis, reactive arthritis and enteropathic arthritis.

The prevalence of spondyloarthritis has been estimated at 0.01-2.5%, with ankylosing spondylitis being the most prevalent.² Extra-articular features include uveitis, psoriasis and inflammatory bowel disease.

The onset of axial spondyloarthritis tends to be before the age of 45 years but it can occur in older age groups, while peripheral spondyloarthritis tends to affect a wider age group.¹

How should patients be monitored?

RISK FACTORS

The association with the HLA-B27 gene is well established. The presence of this gene in the Caucasian population varies from 7.5% in the United States to around 15% in northern Scandinavia, with more than 90% of patients with ankylosing spondylitis possessing this gene. HLA-B27 prevalence in non-Caucasian populations is lower.

The vast majority of patients with ankylosing spondylitis are male, while non-radiographic spondyloarthritis affects both genders equally. Genitourinary (GU) and gastrointestinal (GI) infections with specific pathogens (*Chlamydia trachomatis* and Shigella, »

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Salmonella and Campylobacter, respectively) are recognised triggers for reactive arthritis (see table 1, below).

PRESENTATION IN PRIMARY CARE

Because of the diverse nature of spondyloarthritis, patients can present with a variety of symptoms. Classically, axial spondyloarthritis presents with inflammatory lower back pain of insidious onset, which is typically worse

in the morning and after rest, and improves with activity. In addition, patients can present with alternating buttock (sacroiliac) pain and neck pain and stiffness. The response to oral non-steroidal anti-inflammatory drugs (NSAIDs) is typically good.

Peripheral spondyloarthritis can present with peripheral joint pain and/or swelling, swelling of the digits (dactylitis), tendon and enthesal pain

that is not secondary to a mechanical cause. In these cases, a past medical history or symptoms/signs suggestive of psoriasis, inflammatory bowel disease, uveitis or recent GI or GU infections are of great diagnostic value.

Practical tip 1: Always explore the possibility of inflammatory symptoms in younger patients (< 45 years) presenting with lower back pain and consider early referral if spondyloarthritis is suspected.

Table 1

Risk factors and associations for spondyloarthritis

Spondyloarthritis	HLA-B27	Psoriasis (personal or family history)	Inflammatory bowel disease (personal or family history)	Genitourinary infections	Gastrointestinal infections
Axial spondyloarthritis	✓	✓	✓	✓	✓
Psoriatic arthritis	✓	✓			
Enteropathic arthritis	✓		✓		
Reactive arthritis	✓			✓	✓

Table 2

Modified New York criteria for ankylosing spondylitis⁴

Clinical criteria

- Low back pain and stiffness for more than three months that improves with exercise, but is not relieved by rest
- Limitation of motion of the lumbar spine in the sagittal and frontal planes
- Limitation of chest expansion relative to normal values correlated for age and sex

Radiological criterion

- Sacroiliitis grade ≥ 2 bilaterally or 3-4 unilaterally

Definite AS if the radiological criterion is associated with at least one clinical criterion

REFERRAL

Early referral of patients with suspected spondyloarthritis to specialist care is strongly recommended as this can improve long-term outcomes.

The absence of serological markers, including rheumatoid factor (Rf), anti-cyclic citrullinated peptide (CCP) antibodies and anti-nuclear antibodies (ANA) raises the suspicion of spondyloarthritis in a patient with evidence of inflammatory joint disease.

In the UK, HLA-B27 is present in up to 90-95% of ankylosing spondylitis patients and approximately 50-60% of psoriatic arthritis patients but a negative result does not rule out a spondyloarthritis.³

Inflammatory markers (ESR and CRP) can be elevated in spondyloarthritis but a normal ESR or CRP does not rule out the condition. Joint effusions can be aspirated and analysed to rule out a crystal arthritis. Plain X-rays can be used to assess for long-term joint damage such as erosive disease, syndesmophytes (calcification of the spinal ligaments) or sacroiliitis (see figure 1, p11). However, X-rays can be normal in early disease and therefore MRI may be useful to detect suggestive inflammatory changes of the spine or sacroiliac joints. Ultrasound or MRI can

Table 3

ASAS classification criteria for axial spondyloarthritis (SpA) in patients with back pain for ≥ 3 months and age at onset < 45 years¹

Sacroiliitis on imaging* 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 disease/ulcerative colitis
- Good response to NSAIDs
- Family history of SpA
- HLA-B27
- Elevated CRP

Sacroiliitis on imaging*

- Active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA
- Definite radiographic sacroiliitis according to modified New York criteria

also be used to assess for peripheral subclinical synovitis and enthesitis.

Ankylosing spondylitis has historically been diagnosed using the modified New York criteria (see table 2, opposite).⁴ New classification criteria were developed in 2011 by the American Society of Ankylosing Spondylitis (ASAS), see table 3, opposite.¹

For psoriatic arthritis, CASPAR classification criteria may aid diagnosis, see table 4, below.⁵

There are no specific diagnostic guidelines for enteropathic arthritis but the diagnosis is normally based on the presence of an axial or peripheral spondyloarthritis in the context of a history of inflammatory bowel disease. Similarly, reactive arthritis diagnosis is usually based on the presence of a spondyloarthritis in the context of a recent GI or proven GU infection and in the absence of psoriasis or inflammatory bowel disease.

Practical tip 2: HLA-B27 testing and imaging with plain X-rays are extremely valuable in supporting the diagnosis of spondyloarthritis.

TREATMENT AND MONITORING
Axial spondyloarthritis

NSAIDs (COX-1 and COX-2 inhibitors) are the first-line treatment for axial spondyloarthritis and should be used at the lowest effective dose. The risks and benefits of using NSAIDs should be assessed and gastric protection should be considered.

Patients with intolerance or contraindications to NSAIDs, and patients who do not respond to at least two different NSAIDs at the maximum tolerated dose (2-4 weeks each), should be considered for biologic DMARDs. Biologic treatment response is assessed at 12 weeks and treatment is only continued if there is a reduction in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)⁶ of

at least 50% or 2 points compared with pre-treatment and a reduction in the spinal visual analogue scale (VAS) by 2 cm or more.⁷ If there is an inadequate response to the first biologic therapy, then the patient should be switched to a second anti-TNF-alpha agent, or if they have ankylosing spondylitis/radiographic axial spondyloarthritis, they can be treated with the anti-IL-17 agent secukinumab⁸ (see table 5, p14).

Psoriatic arthritis and other peripheral spondyloarthritis

For patients with psoriatic arthritis presenting with monoarthritis, local steroid injections may be beneficial, and delay the need for DMARD therapy. Standard DMARDs can be offered to patients presenting with oligoarthritis, polyarthritis or persistent monoarthritis. The type of DMARD used depends on the patient's condition and circumstances. Methotrexate and leflunomide should be avoided in patients wishing to conceive, while sulfasalazine should be considered in patients with co-existing inflammatory bowel disease or uveitis. Methotrexate should be first choice in patients with co-existent psoriasis, because of its efficacy in treating both joint and skin disease. NSAIDs, oral, intra-articular or intra-muscular steroids can also be used as adjunct therapies.

Biologic (anti-TNF-alpha) therapy can be considered in patients who are unresponsive to two traditional



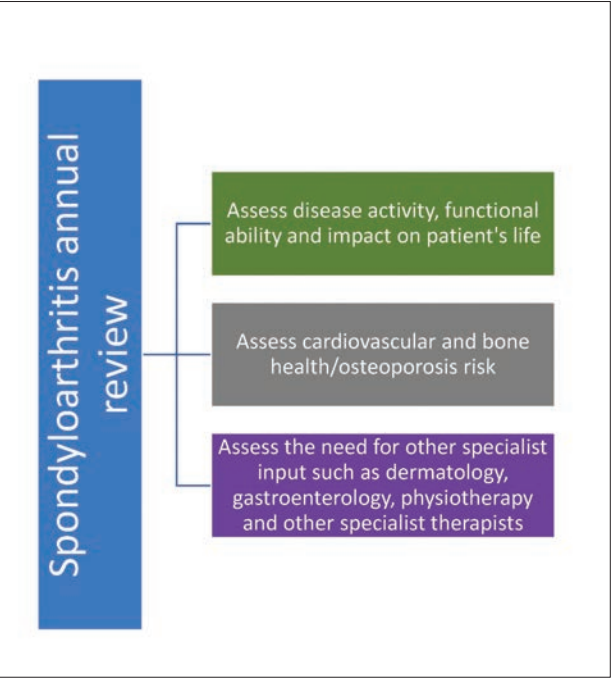
Table 4

CASPAR classification criteria for psoriatic arthritis⁵

A patient must have inflammatory articular disease (joint, spine or entheses) and ≥ 3 points from the following categories:

Category	Description	Points
Current psoriasis or personal or family history of psoriasis	Current psoriasis: skin or plaque disease confirmed by a rheumatologist or dermatologist	2
	Personal history: obtained from patient, family physician, dermatologist, rheumatologist or other qualified healthcare provider	1
	Family history: Presence of psoriasis in first- or second-degree relative as reported by the patient	1
Psoriatic nail dystrophy on current examination	Onycholysis, pitting, hyperkeratosis	1
Negative rheumatoid factor	Any method except latex, but preferably enzyme-linked immunosorbent assay (ELISA) or nephelometry, using local laboratory reference range	1
Current dactylitis (or a history of dactylitis as recorded by a rheumatologist)	Swelling of an entire digit	1
Radiographic evidence of juxta-articular new bone formation	Ill-defined ossification near joint margins but excluding osteophyte formation on plain X-rays of the hand or foot	1

FIGURE 2
Annual review of patients with spondyloarthritis



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DMARDs.^{9,10} In addition, ustekinumab (anti-IL-23/IL-12) or secukinumab can be considered for patients who have not responded to at least one anti-TNF-alpha agent^{11,12} (see table 5, below).

Monitoring of standard and biologic

DMARDs requires regular follow-up in a specialist clinic to assess efficacy, and regular blood test monitoring to assess safety.

Non-pharmacological treatments may include physiotherapy,

hydrotherapy and the use of other specialist therapies such as hand therapy and orthotics.¹³

Stable spondyloarthritis patients can be reviewed annually to assess various aspects of the disease, see figure 2, p13.

Table 5

Mode of action, dose and common side effects of treatments for spondyloarthritis

Drug	Spondyloarthritis	Mode of action	Dose and mode of administration	Half life	Most common side effects/complications include:
NSAIDs: COX-1/COX-2 Inhibitors	AxSpa, PsA, ReA and EA*, but caution in EA	COX-1/ COX-2 inhibition	As per individual medication	As per individual medication	Reflux, peptic ulceration, renal impairment, cardiovascular disease
Methotrexate	Peripheral spondyloarthritis (PsA, EA, ReA)	Dihydrofolate reductase and T-cell inhibitor	7.5-25 mg once weekly PO and SC	3-10 hours	Oral ulceration, nausea, fatigue, alopecia, bone marrow suppression, infections, pneumonitis, hepatotoxicity
Leflunomide	Peripheral spondyloarthritis (PsA, EA, ReA)	Inhibition of dihydroorotate dehydrogenase	10-20 mg OD PO	14 days	Hypertension, leucopenia, infections, nausea, hepatotoxicity, elevated creatine kinase
Sulfasalazine	Peripheral spondyloarthritis (PsA, EA, ReA)	Exact mechanism of action unknown	1 g BD PO	6-8 hours	Nausea, infections, headache, rash, leucopenia, fever
Apremilast	PsA	Inhibitor of phosphodiesterase 4	Titrated up to 30 mg BD	9 hours	Nausea, infections, diarrhoea, headache, depression
Adalimumab	AxSpa, PsA, ReA and EA	Anti-TNF-alpha	40 mg SC every 2 weeks	14 days	Infections, injection site reactions, headache and musculoskeletal pain
Etanercept	AxSpa, PsA, ReA and EA	Anti-TNF-alpha	50 mg SC once weekly	3 days	Injection site reactions, infections, development of autoantibodies, itching and fever
Infliximab	AxSpa, PsA, ReA and EA	Anti-TNF-alpha	5 mg/kg IV every 8 weeks after loading doses	7-9 days	Infections and headache
Certolizumab pegol	AxSpa, PsA, ReA and EA	Anti-TNF-alpha	200 mg SC every 2 weeks after loading doses	14 days	Infections, injection site reactions and rashes
Golimumab	AxSpa, PsA, ReA and EA	Anti-TNF-alpha	50 mg SC once a month	14 days	Infections
Secukinumab	AxSpa and PsA	Anti-IL-17A	150-300 mg SC once a month after loading doses	27 days	Infections, diarrhoea
Ustekinumab	PsA	Anti-IL-12 and anti-IL-23	45-90 mg SC every 12 weeks after loading doses	21 days	Infections, headaches, nausea, diarrhoea, fatigue, injection site reactions

*AxSpa = axial spondyloarthritis, PsA = psoriatic arthritis, EA= enteropathic arthritis, ReA= reactive arthritis

key points

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The spondyloarthritis group is divided into two main subgroups: axial spondyloarthritis and peripheral spondyloarthritis. These may exist as separate entities or coexist in the same patient. Axial spondyloarthritis can be further subdivided into non-radiographic axial spondyloarthritis and ankylosing spondylitis (AS). Peripheral spondyloarthritis encompasses psoriatic arthritis, reactive arthritis and enteropathic arthritis. Axial spondyloarthritis tends to occur before the age of 45 years but can occur in older age groups, while peripheral spondyloarthritis tends to affect a wider age group.

The association with the HLA-B27 gene is well established. The vast majority of patients with AS are male, while non-radiographic spondyloarthritis affects both genders equally. Genitourinary and gastrointestinal infections with specific pathogens (*Chlamydia trachomatis* and *Shigella*, *Salmonella* and *Campylobacter*, respectively) are recognised triggers for reactive arthritis. Classically, axial spondyloarthritis presents with insidious onset inflammatory lower back pain, which is typically worse in the morning and after rest, and improves with activity. Peripheral spondyloarthritis can present with peripheral joint pain and/or swelling, swelling of the digits (dactylitis), tendon and enthesal pain that is not secondary to a mechanical cause.

Early referral of patients with suspected spondyloarthritis to specialist care is strongly recommended as this can improve long-term outcomes. In the UK, HLA-B27 is present in up to 90-95% of AS patients and around 50-60% of psoriatic arthritis patients but a negative result does not rule out a spondyloarthritis.

HLA-B27 testing and imaging with plain X-rays are extremely valuable in supporting the diagnosis of spondyloarthritis. NSAIDs (COX-1 and COX-2 inhibitors) are the first-line treatment for axial spondyloarthritis and should be used at the lowest effective dose. The risks and benefits of using NSAIDs should be assessed and gastric protection should be considered. Patients with intolerance or contraindications to NSAIDs, and patients who do not respond to at least two different NSAIDs at the maximum tolerated dose (2-4 weeks each), should be considered for biologic DMARDs. Monitoring of standard and biologic DMARDs requires regular follow-up in a specialist clinic to assess efficacy, and regular blood test monitoring to assess safety.

Flares can be managed with NSAIDs, or oral, intramuscular or intra-articular steroids depending on the nature of the flare. For patients with coexistent psoriasis, there is a small risk of psoriasis exacerbation with oral steroids.

Practical tip 3: In the absence of contraindications, consider a trial of NSAIDs (COX-1 or COX-2 inhibitors) at the lowest effective dose in patients with suspected spondyloarthritis.

MANAGEMENT OF FLARES

Flares can be managed with NSAIDs, or oral, intramuscular or intra-articular steroids depending on the nature of the flare. For patients with co-existent psoriasis, there is a small risk of psoriasis exacerbation with oral steroids. Advice from the specialist team may be obtained if needed.

COMPLICATIONS

Long-term complications of spondyloarthritis include chronic joint damage and associated chronic disability. Patients with spondyloarthritis are at greater risk of cardiovascular disease and additional risk factors for this should be addressed whenever possible. In addition, spondyloarthritis patients are at increased risk of osteoporosis and fractures and therefore bone health should be optimised with bone protective treatment if needed, including calcium and vitamin D supplements, with or without antiresorptive therapy (bisphosphonates). For the potential complications of treatment, see table 5, opposite.

Practical tip 4: During the assessment of patients with spondyloarthritis, consider reviewing other aspects of the condition including extra-articular manifestations, cardiovascular and bone health, mood and functionality/disability.

CONCLUSION

Spondyloarthritis encompasses a diverse range of conditions that can present with a variety of clinical features. The diagnosis of spondyloarthritis involves clinical assessment, HLA-B27 testing and the use of a variety of imaging modalities including X-ray and MRI. Early recognition and treatment with both pharmacological and non-pharmacological therapies can reduce joint damage and disability and improve long-term outcomes. Regular review is essential for monitoring disease activity, safety and efficacy of treatment, and for the assessment of potential complications.

Competing interests: None

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Further reading

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See also Prompt diagnosis can prevent joint damage in psoriatic arthritis, p17

Useful information

National Ankylosing Spondylitis Society
<https://nass.co.uk/>

Chews Health

The Physio Matters Podcast, Session 26: Solving Spondyloarthropathy with Dr Karl Gaffney
<http://chewshealth.co.uk/tpmpsession26>

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