Spondyloarthritis

Frank McKenna
Consultant Rheumatologist
Trafford General Hospital, Manchester

Editorial

For this issue of Hands On I have asked a rheumatologist with a special interest in spondyloarthritis to write about this common, but often overlooked, aspect of inflammatory joint disease. In particular, I wished to stress the importance of diagnosing inflammatory back pain from among the hundreds of cases of simple, mechanical back pain that are seen in general practice every day.

Now that NICE has allowed biologic drugs to be used in the treatment of both psoriatic arthritis and ankylosing spondylitis it is important to recognise the presenting features of these conditions. Ankylosing spondylitis in particular is difficult to identify and symptoms are often present for years before a definite diagnosis is reached. However, it can now be very effectively treated using biologic drugs and sufferers should no longer develop the crippling spinal deformities with which we are all familiar.

The responsibility for early recognition of symptoms belongs to primary care and I hope that this report will furnish us with the skills to take an effective history and elicit the early signs of spinal inflammatory disease.

Louise Warburton

Introduction

The simplest approach to the diagnosis of musculoskeletal pain is to consider joint diseases in broad categories. The pattern of joint involvement may help to separate soft tissue lesions, such as tendinitis or bursitis, from arthritis. Arthritis is broadly categorised into either inflammatory or non-inflammatory diseases. In the early to mid-twentieth century most inflammatory joint diseases other than gout were considered to be variants of rheumatoid arthritis. Even ankylosing spondylitis was sometimes referred to as rheumatoid spondylitis, and the concept of psoriatic arthritis as a distinct entity was controversial.

In the 1960s a number of family studies led Wright and his colleagues in Leeds to coin the term ‘seronegative spondarthritis’ to link a number of inflammatory joint diseases, including ankylosing spondylitis, psoriatic arthritis, reactive arthritis including Reiter’s disease, enteropathic arthritis (associated with inflammatory bowel disease) and anterior uveitis (iritis). Subsequent studies with the human leukocyte antigen (HLA) B27 have confirmed the genetic association.
A number of features are common to this group of diseases:

- the lack of any association with autoantibodies (including rheumatoid factor) – hence the term ‘seronegative’
- an increased incidence of ankylosing spondylitis in the whole group – hence the ‘spond-’ or ‘spondylo-’ prefix
- an increased family history of associated conditions
- the association with HLA-B27.

The term seronegative spondyloarthritis was preferred but the prefix seronegative has become redundant particularly because of the confusion when used loosely in patients with inflammatory arthritis and a negative test for rheumatoid arthritis. Inflammatory arthritis is now classified into three groups of diseases:

- spondyloarthritis (associated with HLA-B27)
- metabolic arthritis (associated with crystals, e.g. gout)
- connective tissue diseases (associated with antibodies, e.g. rheumatoid arthritis).

Estimates of the prevalence of spondyloarthritis range from 1% to 2% of the population and are similar to the prevalence of rheumatoid arthritis. It may be useful to consider spondyloarthritis as a spectrum of a single disease with differing manifestations. Some patients have multiple features, e.g. a patient with Crohn’s disease (regional ileitis) and a history of iritis and psoriasis developing peripheral arthritis and ankylosing spondylitis. An enthesitis is a feature in some patients, particularly causing Achilles tendinitis or plantar fasciitis. There is a strong familial link with an association with HLA-B27. It is not unusual to find a complex family history with different manifestations of spondyloarthritis in several family members. Undifferentiated spondyloarthritis refers to patients with some features of this group of diseases but without sufficient features for any one diagnosis, for example a patient with synovitis of the knee who may have unilateral sacroiliitis on x-ray and a family history of psoriasis, colitis, iritis or ankylosing spondylitis.

<table>
<thead>
<tr>
<th>Spondyloarthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ankylosing spondylitis</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
</tr>
<tr>
<td>Reactive arthritis</td>
</tr>
<tr>
<td>Enteropathic arthritis</td>
</tr>
<tr>
<td>Undifferentiated spondyloarthritis</td>
</tr>
<tr>
<td>Iritis</td>
</tr>
<tr>
<td>Juvenile spondyloarthritis</td>
</tr>
</tbody>
</table>

**Ankylosing spondylitis**

Ankylosing spondylitis is a chronic inflammatory disease of the axial skeleton; the name is derived from the Greek ‘ankylos’, meaning bent or crooked, and ‘spondylos’, a spinal vertebra. Ankylosis refers to a fibrous or bony bridging of joints and in the spine refers to bridging of one or more intervertebral discs.

**Prevalence**

Ankylosing spondylitis is clinically more common in men than women, with a ratio of approximately 5:1 – although this may partially reflect under-diagnosis in women; approximately 5% of patients presenting with back pain have ankylosing spondylitis. Initial symptoms usually develop from late teens to early 30s although the diagnosis may not be made until later in life. Characteristic symptoms are low back pain with prolonged early morning stiffness that improves with exercise. Some patients may have diffuse pelvic pain and others may have sciatica. It is typical for symptoms to gradually involve the dorsal and then cervical spine but the progress of the disease is variable. A minority of patients develop severe disease with unremitting pain, stiffness and restriction in movement. Some patients will develop episodic synovitis in large joints and approximately 5% require hip replacement, although the majority of patients do not have significant disability.

Characteristic symptoms are low back pain with prolonged early morning stiffness that improves with exercise.
How to differentiate ankylosing spondylitis from mechanical back pain

Although back pain is very common, certain symptoms should alert the clinician to the possibility of ankylosing spondylitis. Back pain that develops with an insidious onset in the second or third decade and improves with exercise is more suggestive of inflammatory than mechanical back pain. Another important symptom is when back pain is associated with prolonged morning stiffness. It is advisable to ask any patient with back pain how long it takes before their back loosens up in the morning. A history of morning stiffness that lasts for an hour or more is an indication of inflammatory disease. A diagnosis of ankylosing spondylitis should also be considered if there is a history of psoriasis, colitis or iritis in the patient or a family history of these conditions.

Recent studies have been undertaken to determine whether other symptoms can help to differentiate mechanical from inflammatory back pain. Night waking, alternating buttock pain, insidious onset and age <40 years at onset have been included in studies where magnetic resonance scanning and HLA testing have been used to detect patients before x-ray changes are established and new diagnostic criteria have been developed.

### Standard criteria for inflammatory back pain
- Age at onset <40 years
- Back pain >3 months
- Insidious onset
- Associated with morning stiffness
- Improvement with exercise
4 out of 5 criteria gives 90% sensitivity.

### New criteria for inflammatory back pain
- Age at onset <40 years
- Insidious onset
- Improvement with exercise
- No improvement with rest
- Pain at night (with improvement on getting up)
4 out of 5 criteria gives 80% sensitivity but all 5 criteria being positive is highly specific for inflammatory back pain.

The recent criteria are similar to established criteria but have excluded morning stiffness and included nocturnal pain. Although prolonged morning stiffness is an important feature of inflammation some patients find it difficult to separate the duration of stiffness from pain, and stiffness that improves in less than an hour of getting out of bed is not helpful in differentiating inflammatory from mechanical back pain. In contrast, a history of nocturnal pain relieved by getting out of bed is not difficult to elicit and was found to be a positive symptom for a diagnosis of inflammatory back pain.

### Physical examination

General examination should be considered for the presence of other causes of back pain, particularly osteoporotic fracture or malignancy including myeloma, prostate and breast. Local tenderness may indicate bone pathology although patients with ankylosing spondylitis may be tender particularly over the sacroiliac joints. Any spinal deformity should be determined, including the presence of scoliosis or kyphosis. Patients with early or mild ankylosing spondylitis may not have any abnormal physical signs, but reduced spinal flexion is common. A modified Schober’s test is a useful measure of restricted flexion in the lumbar spine: a line 10 cm above and 5 cm below the dimples of Venus should increase by more than 5 cm on bending forward as far as possible. Restricted lateral flexion (<10 cms) is also an indication of inflammatory back pain. Chest expansion may be reduced in ankylosing spondylitis: less than 2.5 cm is abnormal. Examination of patients with sciatica or other radicular symptoms should include straight leg raising, femoral stretch test and evaluation of tendon reflexes. The hip joints should be examined for any flexion deformity or restricted rotation.

### Key points on examination

#### Signs of ankylosing spondylitis
- Reduced lateral flexion
- Reduced forward flexion (Schober’s test)
- Reduced chest expansion

#### Signs suggestive of other pathology
- Physical signs of weight loss or anaemia
- Bone tenderness
- Reduced straight leg raising or femoral stretch
- Leg weakness or reduced tendon reflexes

### Investigations

The acute-phase proteins are often raised in ankylosing spondylitis. It is good practice to measure both the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) in any patient.
with back pain, but normal values do not exclude a diagnosis of ankylosing spondylitis. Systemic symptoms, including anorexia, weight loss or night sweats, may raise the possibility of neoplastic disease and would be an indication to measure the blood count, serum calcium, alkaline phosphatase, serum and urinary electrophoresis and the prostate-specific antigen. Although more than 90% of patients with ankylosing spondylitis are HLA-B27 positive, this is also found in approximately 7–8% of Caucasian populations and only approximately 5% of those with HLA-B27 will have ankylosing spondylitis. The HLA-B27 is therefore only helpful as a diagnostic test in borderline cases.

The diagnosis of ankylosing spondylitis is made radiographically but is observer-dependent. A firm diagnosis is made when there is both bilateral sacroiliitis and a spinal lesion – either a syndesmophyte or a corner (Romanus) lesion; these lesions are often subtle and have the appearance of a small erosion or sclerosis at the corner of a vertebra, usually developing initially at the D12/L1 junction. Only 10% of patients develop the appearances of a ‘bamboo spine’ with widespread bridging syndesmophytes at most vertebrae. Sacroiliitis in the absence of a spinal lesion supports a diagnosis of spondyloarthritis but is not specific for ankylosing spondylitis. In early disease, magnetic resonance scanning may detect sacroiliitis or vertebral lesions before these are apparent on plain x-rays.

**Prognosis and management**

The clinical course of ankylosing spondylitis is variable. Although the majority of patients do not have significant disability, employment can be affected, particularly in later life. A minority of patients may develop life-threatening complications including pulmonary fibrosis or aortic valve disease.

All patients should be encouraged to undertake a daily exercise regime and to go swimming regularly. There is often a dramatic improvement from non-steroidal anti-inflammatory drugs (NSAIDs), and these should be continued regularly until there is a remission of symptoms. Proton-pump inhibitors (PPIs) should be co-prescribed in those with risk factors for gastrointestinal complications.

The response to disease-modifying drugs such as sulfasalazine is disappointing except for those with a peripheral arthritis. However, anti-tumour necrosis factor (TNF) drug therapy has revolutionised the lives of patients with severe disease. The majority of patients will respond to anti-TNF treatment although long-term effects are undetermined. The National Institute for Health and Clinical Excellence (NICE) guidance issued in May 2008 (www.nice.org.uk/Guidance/TA143) is that adalimumab or etanercept are recommended as possible treatments for people with severe ankylosing spondylitis who have active spinal disease as assessed on two separate occasions 12 weeks apart, and have tried at least two NSAIDs but they have not worked.

**Psoriatic arthritis**

Psoriatic arthritis occurs in approximately 5% of patients with psoriasis and has an overall prognosis that is better than rheumatoid arthritis. There are 5 different subsets of disease:

- mono- or oligoarthritis
- polyarticular: virtually indistinguishable from rheumatoid arthritis
- ankylosing spondylitis
- distal interphalangeal (DIP) pattern: peripheral synovitis involving the DIP joints in addition to other joints similar to rheumatoid arthritis
- arthritis mutilans: severe destructive arthritis leading to loss of bone and severe deformity.

The management of psoriatic arthritis is similar to that of rheumatoid arthritis and is discussed in Hands On (Series 6) No 3, Summer 2009.
Reactive arthritis

Reactive arthritis is defined as an arthritis that develops following an infection where the organism cannot be recovered from the joint. It usually develops within 2 weeks of a gastrointestinal or urinary infection including Campylobacter, Clostridium, Salmonella, Shigella, Yersinia, or chlamydial infections. The presentation is usually an asymmetrical synovitis affecting the knees or ankles. Approximately 50% of patients are HLA-B27 positive. A dactylitis (sausage finger or toe) is strongly suggestive of reactive arthritis or psoriatic arthritis. Reiter’s disease is a reactive arthritis with specific clinical features. Circinate balanitis or cervicitis and keratoderma blennorrhagica (a rash identical to pustular psoriasis) may occur in addition to the classical triad of arthritis, urethritis and conjunctivitis. Any residual infection should be treated. The management is similar to acute synovitis from any cause and includes analgesics, NSAIDs and intra-articular and/or intramuscular steroid injections. Sulfasalazine or methotrexate may be considered for persistent disease although it is unusual for reactive arthritis to persist beyond 12 months.

Enteropathic arthritis

Episodic peripheral synovitis occurs in up to 20% of patients with either ulcerative colitis or Crohn’s disease, and usually reflects the disease activity in the bowel. Ankylosing spondylitis occurs in approximately 7% of patients with inflammatory bowel disease but spinal disease is largely unrelated to other disease activity. Approximately 50% of patients with inflammatory bowel disease who are HLA-B27 positive will develop sacroilitis. Management is similar to reactive arthritis although more aggressive treatment of the colitis will often lead to improvement in the arthritis.

 Undifferentiated spondyloarthritis

Patients who have some clinical features of the conditions discussed but do not meet specific diagnostic criteria for ankylosing spondylitis, reactive arthritis, psoriatic arthritis and enteropathic arthritis may be diagnosed as having undifferentiated spondyloarthritis. Patients may have symptoms suggestive of inflammatory back pain or have an asymmetric synovitis in addition to either a positive family history, or the presence of psoriasis, iritis, inflammatory bowel disease, enthesopathy and/or radiographic evidence of sacroilitis or a recent history of acute diarrhoea, urethritis or cervicitis.

Management is determined by the severity of disease. In addition to symptomatic treatment with analgesics and NSAIDs, a monoarthritis will usually be managed by intra-articular steroid injection whereas polyarthritis will often be treated with pulse steroids and sulfasalazine or methotrexate.

Iritis

Iritis or anterior uveitis is associated with all the spondyloarthritides. Approximately 50% of patients are HLA-B27 positive. Some patients with a history of iritis may develop episodic large joint arthritis and may be diagnosed as having undifferentiated spondyloarthritis. Management is similar to reactive arthritis.

Juvenile spondyloarthritis

Juvenile inflammatory arthritis may have several heterogeneous clinical presentations. Juvenile spondyloarthritis is uncommon but all of the different clinical manifestations of spondyloarthritis in adults may develop in children. The management of juvenile arthritis is outside the scope of this review, but any child with joint pain should be referred for a specialist opinion.
Conclusion

The spondyloarthritides are an interesting group of related conditions with overlapping features and genetic and familial association. Diagnosis is usually made from clinical features rather than investigations. Symptoms suggestive of inflammatory spinal disease or asymmetrical synovitis in a patient with a history of psoriasis, iritis, inflammatory bowel disease or recent infection should alert the primary care physician to a possible diagnosis of spondyloarthritis and to consider a rheumatological opinion.

References

2. Zochling J, Brandt J, Braun J. The current concept of spondyloarthritis with special emphasis on undifferen-