Seronegative Spondylarthropathies

Dr Robert Marshall
Consultant Rheumatologist, UBHT

Aim & Objectives

Aim
  • To develop an understanding of the seronegative spondylarthropathies

Objectives
  • With reference to the underlying pathology, identify the principal features of ankylosing spondylitis
  • Compare and contrast rheumatoid arthritis and psoriatic arthritis
  • Evaluate the role of HLA-B27 in the pathophysiology of AS

Introduction

This file deals with the seronegative spondylarthropathies (SnSpA), which are a group of inflammatory conditions that mainly affect the spine (spond = spine), but which can also affect the peripheral skeleton.

There are essentially four clinical entities:

  • Ankylosing spondylitis
  • Psoriatic arthritis
  • Reactive arthritis / Reiter’s syndrome
  • Enteropathic arthritis
Although they have different features, and there is a wide spectrum of disease, they share a number of manifestations in common.

**Common Characteristics**

- Absence of Rheumatoid factor (*hence seronegative*)
- Sacro-iliac joint involvement
- Peripheral arthropathy
- Enthesopathy (*see below*)
- Iritis (*inflammation of the iris*)
- Familial tendency - HLA-B27 association

**Enthesopathy**

In contrast with rheumatoid arthritis, where the principal pathological feature is *synovitis*, the hallmark of the seronegative spondylarthropathies is *enthesitis*, or inflammation at the site of ligament, tendon, and capsule insertion into bone (*i.e. at the entheses*). These lesions heal by *fibrosis* and *ossification*, leading over time to formation of bridging *syndesmophytes* and bony fusion (*ankylosis*) of joints.
Ankylosing spondylitis

Case history
A 25 year-old fitness instructor was referred to the Rheumatology clinic with a four-year history of increasing pain in his lower back. He describes a severe burning pain radiating to the buttocks and thighs, which is worse at night and relieved by exercise. He gets up at 5am and goes running, because that is the only way he can find relief from the severe stiffness which he is experiencing. Past history includes a painful red eye, which was treated at the Eye Hospital with drops, and an episode of Achilles tendinitis.

On examination he has a reduced range of movement in his lumbar spine, and is unable to touch his toes. An x-ray of the pelvis shows sclerosis around the margins of both sacroiliac joints. (See images). Blood tests show a normal full blood count, negative rheumatoid factor, but a raised plasma viscosity at 1.96.

A diagnosis of ankylosing spondylitis was made.

(intages courtesy Dr Peter Hollingworth).

Introduction
Ankylosing spondylitis (AS) is the prototype seronegative spondylarthropathy, inasmuch as the other diseases share many of the same features.
Epidemiology

AS typically presents in the 3rd or 4th decade, although occasionally prior to this.

In contrast with most rheumatic diseases, it is 3 times more common in males than in females. The prevalence varies according to the population studied, but in Caucasians it occurs in around 0.2 – 1%. In Haida Indians (native inhabitants of northern Canada) the prevalence is around 5%, whereas it is rare in black Africans.

Aetiology and Pathogenesis

The aetiology is essentially unknown. There is a strong association with the Major Histocompatibility Complex Class I antigen HLA-B27, although other factors including the environment clearly play a part.

HLA-B27 and the Spondylarthropathies

HLA-B27 is an important factor in the pathophysiology of ankylosing spondylitis and the other seronegative spondylarthropathies. In Caucasian populations, an individual with AS has around a 95% chance of possessing HLA-B27. This association is less strong in other ethnic groups. However, it is important to recognize that HLA-B27 is fairly common in the normal, healthy population – in Caucasians, its prevalence is around 10%, and this is even higher for other races.

<table>
<thead>
<tr>
<th>Prevalence of HLA-B27 in different populations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Caucasian</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
</tr>
<tr>
<td>Reactive arthritis</td>
</tr>
<tr>
<td>Enteropathic arthritis</td>
</tr>
</tbody>
</table>

What is the Clinical Use of HLA-B27?

HLA-B27 is of little or no use in assisting the physician in making a diagnosis of AS. The main exception is genetic counselling: HLA-B27 +ve offspring of probands with AS have a 1:3 risk of developing AS themselves.

Why is it Important?
The association between HLA-B27 and the SnSpAs is important, because it gives us valuable insights into the aetiopathogenesis. In the case of Reiter’s syndrome, a genetically-predisposed individual who possesses the HLA-B27 epitope, becomes exposed to a foreign antigen (for example *Chlamydia trachomatis* or *salmonella enteritidis*), and then develops an inflammatory arthritis.

**Molecular Mimicry**

One theory is the concept of *molecular mimicry*: the host mounts an immune response to the invading organism, but the similarity of host antigens to amino acid sequences on the surface of the pathogen results in autoimmune disease. This theory is supported by the finding that there is a certain homology between the *Klebsiella pneumoniae* nitrogenase enzyme and amino acid residues on the B-27 molecule. Other theories exist, but none is entirely satisfactory.

Whatever the trigger for the autoimmune process, activation of T cells leads not only to the release of pro-inflammatory cytokines such as IL-1, IL-6, and TNFα, but also a direct cytotoxic effect. The end result is inflammation, which gives rise to the clinical manifestations of the disease.

**Clinical Features**
Axial Skeleton

Ankylosing spondylitis usually presents in a young male with insidious onset of lower back pain. It will usually be “inflammatory” in nature: that is, it is characteristically burning, radiating to the buttocks and thighs, and associated with severe stiffness. These symptoms are typically worse in the morning (hence early morning stiffness) and on inactivity, and relieved by exercise. This is in contrast to the so-called mechanical back pain, which is worse on movement and relieved by rest.

Non-steroidal anti-inflammatory drugs (NSAIDs) also have a dramatic effect in ameliorating symptoms. As with rheumatoid arthritis, patients’ symptoms will relapse and remit with so-called “flares”.

**Disease Progression**

Recurrent inflammatory attacks lead to increasing stiffness of spinal movement. Reduced lateral flexion is usually the first movement to be clinically detectible, and is also manifest in the cervical spine. In time, the whole spine becomes fused, and the characteristic “question-mark posture” may be noted, with a reduced lumbar lordosis and an exaggerated thoracic kyphosis. In severe cases, patients may have difficulty in seeing straight ahead. (See images)

(Images of normal and ankylosing spondylitis posture)

*(image on right courtesy Dr Peter Hollingworth).*

Peripheral joints

Around 20% of patients with AS develop peripheral joint involvement. This is usually an asymmetrical large joint oligoarthritis (e.g. hips and knees). Histologically, synovitis is
often seen, but this may be a secondary phenomenon to an initial enthesitis at the site of capsule insertion.

Insertional Tendinitis

AS does not only affect joints. Other entheses such as the Achilles tendon, and the plantar fascia may be affected. Patients will complain of pain and localized tenderness in the Achilles tendon or heel respectively. With repeated attacks, bony spurs may be seen on plain radiographs. An example is shown below.

Plain radiograph of a sagittal section of the heel of a patient with AS, showing a calcaneal spur (boxed). Taken from Rheumatology by Klippel and Dieppe 3.27 Fig. 3.27.4A

Extra-articular manifestations

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constitutional</td>
<td>Low-grade fever</td>
</tr>
<tr>
<td></td>
<td>Malaise</td>
</tr>
<tr>
<td></td>
<td>Fatigue</td>
</tr>
<tr>
<td></td>
<td>Weight loss</td>
</tr>
<tr>
<td>Eyes</td>
<td>Attacks of anterior uveitis in 25 – 30% (painful red eyes)</td>
</tr>
<tr>
<td>Heart</td>
<td>Aortic incompetence</td>
</tr>
<tr>
<td></td>
<td>Conduction defects (both rare)</td>
</tr>
</tbody>
</table>
Clinical Assessment

The overall appearance of the spine and its posture should be noted. Spinal movements should be assessed, starting with the cervical spine. Lateral flexion is the movement that is usually affected early on in the disease process.

Modified Schöber’s test

This is often used to assess spinal mobility. Examining the patient from behind, the “dimples of Venus” overlying the posterior superior iliac spines are identified. The midpoint between these two dimples represents the lumbosacral junction: a mark is made 5cm below this point, and another mark is made 10cm above. The patient is then asked to bend forward and attempt to touch the toes. The distance between the two marks is then reassessed: in a normal individual, the 15cm should extend by at least a further 5cm. In AS, it will usually not extend significantly.

Localised tenderness is sometimes elicited over the sacroiliac joints. Peripheral joints should also be examined for evidence of involvement, and attention should be paid to commonly affected entheses such as the Achilles tendon and the plantar fascia. General examination should include an inspection of the eyes, and auscultation of the heart and lungs.

Regular Monitoring

It is often helpful to record the following measurements in order to assess disease progression:

- Finger-floor distance (with patient bending forwards)
- Wall-occiput (patient standing with back to wall and neck fully extended)
- Chest expansion in 5th intercostal space
- Cervical movements

Investigations

A plain radiograph of the pelvis is often the only radiological investigation that is required to assist in diagnosis. Sacro-iliac joint involvement is seen as sclerosis around the margins of the joints, which is often bilateral. The pubic symphysis is sometimes also
affected. With advanced disease, ascending spread may be noted in the lumbar spine, with Romanus lesions, syndesmophyte formation and, in established cases, the so-called “bamboo spine”. (See images)

If plain radiographs are unhelpful, as may be the case in early disease, CT or MRI of the SI joints may occasionally be used.

Blood tests should include the following:
- Full blood count
- Plasma viscosity or ESR
- Rheumatoid factor
- C-reactive protein
- Urea and electrolytes
- Liver function tests
- Bone profile
- Thyroid function

FBC may show the anaemia of chronic disease, and the inflammatory markers (ESR, PV, CRP) will be raised. Rheumatoid factor is negative. Certain metabolic abnormalities may mimic rheumatic disease, hence the need for the remaining tests.

If pulmonary or cardiac involvement is suspected, then spirometry (and formal pulmonary function tests), chest radiograph, ECG, and echocardiogram may be indicated.

Treatment
Advice and Education

It is critically important to inform patients of their diagnosis, and to work with them to manage their disease – after all, it is they who have to live with it every day. Information leaflets are available in most outpatient clinics from the Arthritis Research Campaign, and many patients seek information on the Internet. (See www.arc.org.uk for starters). Many self-help groups exist: the National Ankylosing Spondylitis Society (NASS) is a nationwide organization with many local groups that meet regularly.

Exercise and Physiotherapy

Perhaps the most important aspect of disease management is regular exercise. Patients should be referred to a physiotherapist (preferably one with specialist knowledge) for instruction about correct forms of exercise, and should be encouraged to perform these at least once per day. Hydrotherapy, or even just swimming, is a valuable mode of treatment as the added buoyancy allows for non-weight-bearing exercise.

Pain Relief

Non-pharmacological methods such as warm showers or baths in the morning (when the stiffness is maximal) can be extremely helpful. Hot packs and topical analgesics can provide localized relief. Some patients find acupuncture helpful.

Non-steroidal anti-inflammatory drugs (NSAIDs) are extremely effective in relieving not only the pain but also the stiffness of inflammatory arthropathies. Patients should be encouraged to take the drugs regularly, as the anti-inflammatory effect is cumulative. Simple NSAIDs such as diclofenac may be tried initially, but preparations such as indomethacin and nabumetone are more potent. If gastro-toxicity is a problem, then the newer COX-2 selective agents may be helpful.

Local corticosteroid injections into joints and tendon sheaths may provide symptomatic benefit.

Second-line Therapy

Second-line agents are rarely used in AS in the United Kingdom, as there is no evidence to suggest that they alter the progression of the spinal disease. The exception, however, is patients who have problematic peripheral joint disease (e.g. knees and hips) – these individuals may derive benefit from either sulphasalazine or methotrexate.

Research is currently underway to identify whether there is a role for the anti-TNFα agents in AS.
**Summary of Treatment Options in AS**

<table>
<thead>
<tr>
<th>Advice and Education</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise and Physiotherapy</td>
</tr>
<tr>
<td>Anti-inflammatory Drugs (NSAIDs / COX-2)</td>
</tr>
<tr>
<td>Second-line therapy?</td>
</tr>
</tbody>
</table>

**Prognosis**

The prognosis in ankylosing spondylitis is extremely variable. Some patients may suffer progressive rigidity of the spine, associated with severe destructive peripheral arthritis, whilst others may simply undergo episodic flares of inflammatory back pain, without major progressive deformity. Predicting prognosis may be difficult, but age of onset before 21, and peripheral joint involvement (especially hips) confers a worse prognosis.

**Psoriatic Arthritis**

**Case History**

A 36 year-old man presented to the Rheumatology clinic with a six-month history of painful swollen knees. He indicated that his right knee initially became swollen soon after a long walk, and he found it difficult to move. Soon afterwards, his other knee had swollen up, although this had since settled. More recently, however, he had developed some swelling in the joints of his hands, which made it difficult for him to play the guitar.

On examination, he had multiple nail pits, with psoriasis of the scalp and in the natal cleft. He had synovitis of the distal interphalangeal joints of two fingers, and his entire right fourth toe was swollen (*dactylitis*). Both knees had large effusions.
Blood tests revealed a raised plasma viscosity (1.88). A diagnosis of psoriatic arthritis (PsA) was made.

Introduction

Psoriasis affects 2-3% population, and joint disease occurs in around 15-20% of these. Although in many cases the skin disease may be well-established, in a proportion of cases of psoriatic arthritis the skin disease may be minimal at presentation, and may be restricted to areas such as the scalp, nails, natal cleft and extensor surfaces of the elbows and knees. Indeed, the joint disease may precede the skin disease by months or even years in some patients. Interestingly, nail pits occur in around 90% of patients with psoriatic arthritis, but in only 40% of patients with skin disease alone.

Epidemiology

Males are affected equally frequently as females. The disease usually presents in the 3rd and 4th decades of life.

Clinical Patterns

Psoriatic arthritis occurs in several different forms:

- Asymmetric oligo- or polyarthritis (60%)
- Spondylarthropathy (10 - 40%)

(slides courtesy Dr Peter Hollingworth)
- DIP joint disease / dactylitis (10%)
- Arthritis mutilans with sacroiliitis (5%)
- Symmetrical polyarthritis (indistinguishable from rheumatoid but seronegative)

Asymmetric oligo- or polyarthritis

The case history outlined above is perhaps illustrative of the first subgroup of PsA patients, which represents the majority. These patients develop inflammation of a few (oligo = few) joints in an asymmetric fashion. These will relapse and remit, and are often initially managed conservatively with NSAIDs and local injections. In many patients, however, second-line therapy is used at some stage.

Spondylarthropathy

This group develop a disease which is clinically indistinguishable from ankylosing spondylitis, but in the presence of psoriatic skin disease. It is managed in the same way as AS.

DIP joint disease / dactylitis

A small proportion of patients show a disease pattern whereby mainly the distal interphalangeal (DIP) joints of the fingers and toes are affected. Some digits may develop a dactylitis, which indicates inflammation of the entire digit – interphalangeal joints in addition to tendon sheaths. This is sometimes referred to as a sausage digit. The image below shows DIP joint disease (slide courtesy Dr Peter Hollingworth).

Arthritis mutilans with sacroiliitis
About 5% of patients develop *arthritis mutilans* in addition to sacroiliitis. This, as might be expected, is a grossly destructive arthropathy, which results in a “telescoping” phenomenon (i.e. shortening of the digits). This can be seen in the image below, which also shows characteristic psoriatic skin disease on the extensor surfaces of the knees, along with swollen knee joints.

(image courtesy Dr Jaya Ravindran)

Radiologically, the telescoping phenomenon is often termed a “pencil-in-cup” deformity, as the proximal phalanx erodes into the adjacent bone. This can be seen below.
Symmetrical polyarthritis

A final subgroup develop a symmetrical arthritis which is indistinguishable from rheumatoid arthritis. This will be seronegative (i.e. without the presence of rheumatoid factor). The precise proportion of patients is extremely difficult to estimate. Treatment is the same as for rheumatoid arthritis.

Investigations

Blood tests
As with most rheumatic diseases, the full blood count will usually show the anaemia of chronic disease (normocytic, normochromic). There may also be a mild leukocytosis. The inflammatory markers (ESR, PV, CRP) will be raised. Rheumatoid factor and autoimmune profile will be negative.

Radiology
The changes affecting the sacroiliac joints and the lumbar spine have already been described in the section on ankylosing spondylitis. Subtle differences do exist, for example sacroiliitis is more likely to be unilateral in PsA, but further elaboration is beyond the remit of this discussion.

A useful way of approaching the radiological features of psoriatic arthritis is to compare its appearance on hand and feet x-rays with that of rheumatoid arthritis:

- The pattern of PsA is different. DIP joints are often affected, and are characteristically spared in RA.
- The arthritis is asymmetrical, whereas RA usually affects widespread MCP / MTP joints and PIP joints.
- Periarticular osteopenia is absent in PsA
- In PsA there is a tendency to ankylosis (fusion) of the joint
- “Pencil-in-cup” deformities are seen in PsA (see above)
- Proliferative bone formation around marginal erosions, particularly at the terminal phalanges.
Treatment

The basic principles of education, exercise, and NSAIDs are the same as for ankylosing spondylitis. Local corticosteroid injections (intra-articular and into tendon sheaths) are commonly used to treat local areas of inflammation.

Second-line therapies are more commonly used, particularly where there is peripheral joint involvement, as there is better evidence that these provide symptomatic and functional benefit in the long term when disease is not controlled by NSAIDs. Agents used include sulphasalazine, methotrexate, intramuscular gold injections, azathioprine, and cyclosporin. The role of anti-TNFα and other “biological” agents is currently being evaluated.

Reactive arthritis / Reiter’s Syndrome

Case History

A 22-year old student presented with a one month history of pain and swelling in his left wrist, left knee, and both ankles. The symptoms had developed without warning over the course of two days. He also complained of watery red eyes, and on direct questioning he admitted to some urethral discharge. He mentioned that he had recently returned from a weekend in Amsterdam where he had had casual sex.

On examination, he had synovitis of his wrist, knee, and ankles, and bilateral conjunctivitis. There was a painless rash on the glans penis, and an obvious urethral discharge. Urethral swabs confirmed the presence of *Chlamydia trachomatis*. 
A diagnosis of Reactive arthritis was made. He was treated with tetracycline for the *Chlamydia*, and indomethacin for the arthritis. His symptoms gradually settled over the next six weeks, and by three months he was almost back to normal.

### Introduction

Reactive arthritis is often termed Reiter’s Syndrome, after Hans Reiter who in 1916 described a triad of *urethritis, conjunctivitis*, and *arthritis* that occurred in an officer after a dysenteric illness. A modern definition might be as follows:

> “An episode of peripheral arthritis of more than one month’s duration occurring in association with urethritis / cervicitis or diarrhoea”

### Epidemiology

The annual incidence of reactive arthritis is difficult to estimate, but is of the order of 30-40 / 100000. It occurs most frequently in young adults in the age range 20 – 40, and is probably equally common in men and women. Its occurrence is worldwide, and tends to cluster in families.

Reactive arthritis and HLA-B27

Reactive arthritis is strongly associated with HLA-B27. Between 65 – 95% of patients are HLA-B27 positive, and conversely, individuals with HLA-B27 have a greatly increased risk of developing reactive arthritis during their lifetime; this relative risk may be as high as 50-fold. However, reactive arthritis can occur in the absence of HLA-B27, and also HLA-B27 positive individuals do not necessarily develop arthritis when exposed to triggering pathogens.
Thus clinically, although it is sometimes helpful to test for HLA-B27 in a patient with suspected reactive arthritis, the result should be interpreted with caution as it does not alone confirm or refute a diagnosis.

Aetiology and Pathogenesis

This has been discussed in some detail in the section on ankylosing spondylitis. Suffice it to say that reactive arthritis is perhaps the prototype condition which gives rise to theories of the pathogenesis of many of the inflammatory arthropathies, because there is a clear interaction between genetic factors (HLA-B27), and environmental factors (infecting organisms). No theory is entirely proven, but molecular mimicry is one possibility.

Implicated organisms

A multitude of organisms have been implicated. The most common are listed below.

<table>
<thead>
<tr>
<th>Genitourinary Tract</th>
<th>Gastrointestinal Tract</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Chlamydia trachomatis</em></td>
<td><em>Salmonella enteritidis</em></td>
</tr>
<tr>
<td><em>Neisseria gonorrhoeae</em></td>
<td><em>Campylobacter jejuni</em></td>
</tr>
<tr>
<td><em>Mycoplasma fermentens</em></td>
<td><em>Cryptosporidium</em></td>
</tr>
<tr>
<td></td>
<td><em>Shigella flexneri</em></td>
</tr>
<tr>
<td></td>
<td><em>Enterotoxigenic E. coli</em></td>
</tr>
</tbody>
</table>
Clinical Features

Articular symptoms

The typical presentation is of an acute asymmetrical oligoarthropathy that occurs within days or weeks of an acute infection of the genitourinary or gastrointestinal tract. Typically, large weight-bearing joints such as hips, knees and ankles are affected, but involvement of the shoulders, elbows, wrists, and even the small joints of the hands may occur. Back pain is rare at initial presentation, but in patients whose disease becomes recurrent, this may be a feature, and sacroiliitis may be seen radiologically.

Extra-articular disease

Although it is often the joint symptoms that bring patients to medical attention, reactive arthritis is a systemic disease. Constitutional features such as fatigue, and a low-grade pyrexia may occur. Various tendinitides, tenosynovitides, and other enthesal conditions such as plantar fasciitis may occur.

Mucocutaneous features are common. A variety of lesions are seen in the mouth. Painless plaque-like rashes on the glans penis (*circinate balanitis* – see image under case history above) occur in men, and a rash on the hands and feet that resembles pustular psoriasis (*keratoderma blenorrhagicum*) is often seen.

Keratoderma blenorrhagicum (Image courtesy Dr Peter Hollingworth)
Ocular lesions are also common. A sterile conjunctivitis occurs frequently, and more persistent cases may progress to an acute anterior uveitis (*iritis*). In these cases pain, redness of the eyes, and photophobia are seen; ophthalmological assessment is mandatory.

Rarely, cardiac and renal involvement may occur.

A summary of the clinical features is shown in the table below.

<table>
<thead>
<tr>
<th>Clinical Features of Reactive Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organ System</strong></td>
</tr>
<tr>
<td>Constitutional</td>
</tr>
<tr>
<td>Joints</td>
</tr>
<tr>
<td>Soft tissues</td>
</tr>
<tr>
<td>Eyes</td>
</tr>
<tr>
<td>Mucocutaneous</td>
</tr>
<tr>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>Other (rarely)</td>
</tr>
</tbody>
</table>

**Investigations**

As with most rheumatic diseases, the full blood count will usually show the anaemia of chronic disease (*normocytic, normochromic*). There may also be a mild leukocytosis. The inflammatory markers (ESR, PV, CRP) will be raised. Rheumatoid factor and autoimmune profile will be negative.

An ECG should be performed, as should urinalysis. Affected joints should, if possible, be aspirated and the synovial fluid sent for Gram stain, microscopy, culture, and exclusion of crystals. If appropriate, urethral swabs and stool culture should be sent.

HLA-B27 antigen, or HLA typing, is occasionally useful once the acute symptoms have settled.
Treatment

Non-steroidal anti-inflammatory drugs (NSAIDs) are the treatment of choice, and should be given regularly to maximize the anti-inflammatory effect. If there is any evidence of ongoing genitourinary or enteric infection, then this should be treated appropriately with antibiotics. This is, however, unlikely to improve the arthritis itself.

Once infection has been excluded, intra-articular glucocorticoids will effectively treat any joint inflammation. In severe cases, systemic glucocorticoids may be used, but long-term use (more than a few weeks) is not recommended.

Ocular inflammation should be referred to an ophthalmologist for prompt diagnosis and treatment.

Persistent cases may warrant second-line therapy, although this is the exception rather than the rule. Drugs used include sulphasalazine and methotrexate.

Prognosis

In the majority of cases, the prognosis is good, and symptoms will settle completely within a few weeks to months. However, around 50% of patients will have one or more relapses, which should be treated in the same fashion as an acute attack. Lasting joint damage is rare.

Enteropathic Arthritis

Case History

A 46-year old woman was referred from the gastroenterology ward. She had suffered with ulcerative colitis for 15 years, and had recently undergone a relapse of her symptoms. Whilst on the ward, her knees had become painful and swollen, and she had developed a painful heel, which made walking uncomfortable. On more direct questioning, she mentioned that she had suffered with a burning lower back pain for the last five years, which was associated with around two hours of early morning stiffness. She had not thought much of this, as it had generally occurred at times when her colitis was bad.

The gastroenterology team had aspirated both of her knees, and microscopy and culture of the synovial fluid showed no organisms. The sample was also negative for crystals. On review of her recent barium enema, there is fusion of the sacroiliac joints suggestive of long-standing sacroiliitis. (Image courtesy Dr Peter Hollingworth)
Introduction

In common with many other autoimmune diseases, the features of inflammatory bowel disease (ulcerative colitis and Crohn’s disease) are not confined to the gut. Arthritis is probably the commonest extra-intestinal manifestation; other features include acute anterior uveitis, and cutaneous features such as erythema nodosum and pyoderma gangrenosum.

Epidemiology

The prevalence of ulcerative colitis is around 75 per 100,000 population, and that of Crohn’s disease is about the same again. Arthritis occurs in up to 20% of these individuals. Men and women are equally affected.

Clinical Features

Two patterns of joint disease are recognized, although there is often overlap between the two.

Peripheral oligo-arthritis
This generally affects the joints of the lower limb such as hips and knees, and is usually non-erosive. Enthesitis (such as plantar fasciitis) may also occur. The arthritis is more commonly associated with Crohn’s disease than ulcerative colitis, and usually flares with the activity of the bowel disease; indeed, resection of the colon in UC may cure the joint symptoms. This form of arthritis is not associated with HLA-B27.

Sacro-iliitis with spondylitis

This is clinically indistinguishable from ankylosing spondylitis, and is associated with HLA-B27 in 60-70% of cases. The joint disease may predate the intestinal disease by some years, and its course is independent of bowel activity.

Investigations

Blood tests

As with most rheumatic diseases, the full blood count will usually show the anaemia of chronic disease (normocytic, normochromic), although in established intestinal disease, there may be a concomitant iron-deficiency. There may also be a mild leukocytosis. The inflammatory markers (ESR, PV, CRP) will be raised. Rheumatoid factor and autoimmune profile will be negative.

Radiology

The changes affecting the sacroiliac joints and the lumbar spine are indistinguishable from those seen in ankylosing spondylitis. The peripheral joints will show soft tissue swelling, but generally an absence of erosions.

Treatment

NSAIDs are effective, but unfortunately they often cause a flare of colitis so their use is limited. Simple analgesics will provide pain relief, but do not treat the inflammatory component.

Exercise, physiotherapy, and non-pharmacological methods such as hot and cold packs should be encouraged. Intra-articular glucocorticoids are effective for the peripheral joints, but oral preparations should only really be given for the bowel disease, and not for the arthritis.

Second-line agents are sometimes used, but the only drug that is of any proven benefit is sulphasalazine, which is also used for the treatment of colonic involvement.