

Inflammatory Disorders of the Spine

Victor N. Cassar-Pullicino

Department of Radiology, The Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry, UK

Introduction

The underlying pathology of target organs in spinal inflammatory disorders dictates the imaging appearances throughout the natural history of the disease processes. Although overlap exists, inflammatory disorders can predominantly affect the synovial articulations of the spine (rheumatoid disease) or primarily the entheses of ligaments and intervertebral discs (seronegative spondyloarthropathies). The various disease states are not static but rather need to be viewed as dynamic and progressive, usually resulting in complications. In rheumatoid disease it is primarily the cervical spine that is involved, but it is very rare that the rheumatoid arthritis patient presents with cervical spine manifestations as the first mode of presentation. On the other hand seronegative spondyloarthropathies usually present with axial manifestations of enthesitis as the first mode of presentation, and these are easily overlooked.

Synovial involvement of the cervical spine in seropositive inflammatory states has a predilection for the facet joints, and in particular the C1-C2 articulations. In seronegative spondyloarthropathy, the inflammatory site is the entheses where the collagen of the ligaments or intervertebral disc annulus enters bone directly. The cause of the inflammatory process is the generation of cytokines, which results in edema, bone erosion, disorganization of bone and ligament structure, which promotes a reactive osteitis and eventually ossification of the ligaments commencing at the entheses interface. Histologically, the inflammatory enthesitis reveals a macrophage-predominant cellular infiltrate consistent with the knowledge that tumor necrosis factor (TNF)- α , which is a pro-inflammatory cytokine produced by macrophages, plays a key role in the inflammatory spondyloarthropathies. The seronegative spondyloarthropathies can be further categorized based on the imaging findings equated to the clinical features and laboratory findings. Although multiple modalities such as radiography, computed tomography (CT) and scintigraphy can be employed to assess the inflammatory sites within the axial and the appendicular skeleton, it is primarily

magnetic resonance imaging (MRI) that is the optimal imaging modality to assess inflammatory disorders of the spine because of its high sensitivity and specificity. Although contrast-enhanced magnetic resonance (MR) studies are not usually required for diagnosis, they can distinguish between active and inactive disease and also help in assessing the response to anti-inflammatory therapy.

Clinical Features

The etiology of the inflammatory spondyloarthropathies is still unknown, although the human leukocyte antigen (HLA-B27) is found to be present in 90% of patients suffering from ankylosing spondylitis, 50% patients with reactive arthritis (previously known as Reiter's syndrome) and only 20% of patients with psoriasis. Inflammatory back pain that is worse at night and in the early morning is the key clinical hallmark of inflammatory spondyloarthropathy. Ankylosing spondylitis usually presents with early morning stiffness that is eased by movement and exercise. However the onset is usually insidious allied with multiple relapsing episodes of back pain that usually starts in the lumbar spine. The condition can remain undiagnosed for years, resulting in fusion of the spine, which renders the condition painless. Although classification subtypes have evolved over the last 30-40 years, the main challenge facing the radiologist is the early diagnosis of inflammatory spinal disorders because the early institution of therapy can limit disability and diminish disease progression. MRI has not only helped in the early detection of disease, but also is increasingly being employed in scoring mechanisms that without doubt will be incorporated in time in decision-making therapeutic protocols.

Sacroiliitis

Sacroiliitis is the hallmark of all spondyloarthropathies. It is a fundamental component required in establishing

the diagnosis of ankylosing spondylitis, but it is also relevant to the other spondyloarthropathies. In ankylosing spondylitis it is bilateral and symmetrical, while in psoriatic spondyloarthropathy and reactive arthritis it can be bilateral or unilateral. Involvement of the axial skeleton is unusual and indeed rare in the absence of sacroiliitis.

Conventional radiography remains the initial diagnostic imaging modality recommended despite its low sensitivity and relatively high false-negative rate in early disease. There are inherent limitations to the proper radiographic assessment of the sacroiliac joints; these arise because the joints themselves are divergent in the anteroposterior projection, which is why a posteroanterior projection is usually a better option of assessing the sacroiliac joints. It is also well known that conventional radiography can miss advanced sacroiliitis. Early inflammatory sacroiliitis can result in a loss of the sharpness of the subchondral bone outline of the joint; this then progresses to becoming irregular due to the presence of erosions, and this in turn produces an appearance of localized joint widening. Sclerosis of the subchondral bone on either side of the joint is fairly diagnostic in established disease, especially when it involves the inferior and middle portion of the joint and is more pronounced on the iliac side. However, in established disease, the sacroiliac joint can also exhibit loss of sharpness due to ossification across the joint leading to ankylosis. The modified New York criteria have identified five radiographic stages of sacroiliac joint involvement:

Grade 0: no abnormality

Grade 1: suspicious changes

Grade 2: sclerosis with early erosions

Grade 3: severe erosions, pseudo joint widening and partial ankylosis

Grade 4: complete ankylosis.

In practice, however, radiological detection of these changes is challenging with poor interobserver and intraobserver reliability for the changes in early disease, namely stages 1 and 2.

The relatively late development of radiographic changes in ankylosing spondylitis is undeniably one of the factors that can delay the diagnosis. However, MRI has revolutionized the early diagnosis of sacroiliitis. This is primarily dependent on the pericardilage osteitis, which is an important feature of ankylosing spondylitis and produces bone marrow edema that is well picked up on the edema-sensitive sequences such as T2-weighted sequences with fat suppression or the short tau inversion recovery (STIR) sequence. T1-weighted spin-echo sequences are, however, better at depicting articular erosions. The degree of the edema can vary, ranging from florid, fairly extensive areas of periarticular edema to more focal and localized zones of edema paralleling the joint line. It is usually the inferior iliac portion of the joint that is involved in the early stages of sacroiliac inflammatory change. Gadolinium-enhanced MR studies have been advocated in active disease, as there is a rise in the MR signal at the point of enhancement in the joint space

and periarticular tissues in the first 2 min. However, contrast enhancement is particularly useful if the edema-sensitive sequence (STIR) is equivocal. Using contrast enhancement, MRI can not only distinguish active from inactive disease, but it can also monitor the treatment response where a decrease in the enhancement even in the persistent presence of bone marrow edema has been shown to be strongly correlated with a good clinical response to treatment. There are various ways of utilizing post-contrast MRI in the assessment of sacroiliac disease. They are particularly helpful in determining whether the instituted drug regime is working, identifying a need to alter the drug regime, and deciding to stop drug regimes if they are not working in view of the significant side-effects and high cost.

Although the edema-sensitive sequences, in particular the T2 sequences with fat suppression, are very sensitive and specific in visualization of bone marrow edema, joint widening and joint fluid, they are not as good in identifying subtle erosions because of the relatively low spatial resolution compared with CT. The high spatial resolution inherent in CT identifies subtle erosions and subchondral sclerosis in sacroiliac joint involvement. CT indeed is the preferred modality for the detection of very early erosions of the sacroiliac joints and their early ankylosis. However, one needs to bear in mind that sclerosis on its own can have a similar appearance in both active disease and in burnt-out inflammation.

Axial Skeleton

Ankylosing spondylitis is the seronegative spondyloarthropathy prototype. It is primarily a disease of the axial skeleton involving the sacroiliac joints and the spine. The primary target organ is the enthesis where the spinal longitudinal ligaments and annulus fibrosus merge directly with the bone. In the early manifestations of inflammation an osteitis is produced by the inflammatory response, and this leads to bone marrow edema and then subsequently this is followed by reactive sclerosis and eventually ossification of the involved ligaments. There is usually an orderly progression of involvement of the spine commencing first in the thoracolumbar and lumbosacral regions, and then advancing to the midlumbar, midthoracic and eventually the cervical spine.

Spondylitis

Spondylitis occurs in about 50% of ankylosing spondylitis patients, although females are relatively less affected. The earliest changes are caused by enthesitis at the insertion of the outer fibers of the annulus fibrosus on the ring apophysis of the vertebral end plate. Although this occurs circumferentially, it is predominantly the anterior attachment that usually produces the more florid manifestations. Subtle erosions with reactive sclerosis in the vertebral corners are seen, and radiographically these

have been referred to as Romanus lesions when viewed as erosions, and “shiny corners” when the erosion is associated with sclerosis due to the reactive osteitis. The Romanus erosive disease can also produce an apparent squaring of the anterior outline of the vertebral body. However, the Romanus lesions are short lived and resolve by producing resultant syndesmophyte formation. The syndesmophytes represent the ossification of the outer fibers of the annulus fibrosus in ankylosing spondylitis. They are seen radiographically as very fine and symmetric in appearance, bridging the intervertebral space. This may initially appear at a single disc level, but usually progresses to involve multiple segments producing the so-called characteristic “bamboo spine”. The same inflammatory process results in ossification of the longitudinal ligaments, which insert onto the vertebral bodies producing squaring of the vertebral body appearance as the fusion progresses.

MRI is the most sensitive diagnostic tool for the identification of discovertebral inflammatory disease. The Romanus lesions are identified on the sagittal sequences and characterized by a triangular pattern of bone marrow edema at the corners of the vertebral end plates highlighted by low T1 signal and high T2 fat-saturated and STIR sequence appearance. The small erosion can be overlooked when compared with the areas of edema. After the acute Romanus lesion phase subsides, the chronic lesions are identified by a fatty marrow replacement at the sites of enthesitis inflammation within the vertebral bodies, highlighted by a high T1 signal and a low signal on STIR and T2 fat-saturated sequences. Multiple contiguous areas of high T1 signal can be seen in vertebral bodies and in particular at their corners in segments of the spine that have undergone extensive fusion. The intervertebral disc in cases of long-term spinal fusion can also undergo changes producing a high T1 inherent MR signal. This has been related to the presence of calcification or alternatively the presence of marrow within mature transdiscal ankylosis.

Contrast-enhanced MR studies and diffusion-weighted MR sequences have also been employed in the detection of inflammatory disease of the spine. They can be useful in the acute phase of inflammatory change, particularly in the early manifestations of the disease. In acute Romanus lesions, contrast medium injection usually renders the erosions more clearly defined. However, comparative studies with STIR sequences have concluded that there is very little advantage as both have high intraobserver and interobserver reliability and more active lesions are seen on the STIR sequences. In cases where the STIR sequence is equivocal, dynamic gadolinium diethylenetriaminepentaacetate dextran (DTPA) studies have been found useful.

Although there is no doubt that MRI has revolutionized the role of imaging in the early and active phases of inflammatory disorders of the spine, one also needs to bear in mind that it does have a particular drawback in identifying the syndesmophytes that are the hallmark of established disease. Syndesmophytes are not well seen by

MRI and easily overlooked because the low signal of the syndesmophyte is similar to the low signal of the normal anterior longitudinal ligament and annulus fibrosus. Similarly MRI can overlook ossification and fusion of other spinal elements, namely the apophyseal joints, paraspinal ligaments and interspinous ligaments. It is still the case that radiographic diagnosis is very easy when compared with MRI in the chronic case where there is established soft tissue ossification.

Spondylodiscitis

There are two types of spondylodiscitis that can be detected within the discovertebral junction. Primary spondylodiscitis, or as it is sometimes known Andersson type A lesions, resembles Schmorl’s nodes exhibiting a rim of edema within the vertebral body, a focal endplate defect and enhancement of the marrow edema. The primary spondylodiscitis is usually a sign of early discovertebral involvement with a stable spinal status. In the secondary spondylodiscitis, or as it is sometimes known Andersson type B lesions, there is more extensive and florid discovertebral disease and destruction. These are particularly well demonstrated on CT and MRI. The degree of vertebral destruction is usually mild, but there is often extensive bony edema and bony sclerosis, and in long established cases the endplates can be completely destroyed on both sides of the intervertebral disc. In Andersson type B lesions the spine is unstable at the site of involvement because of increased mobility. This increased mobility could be at a level between fused segments or be associated with deficiency of the posterior elements where there is a pseudoarthrosis due to a fracture. It is therefore imperative that the posterior elements are assessed assiduously to differentiate type A from type B Andersson lesions, as the latter are associated with pain and instability and can give rise to neurological dysfunction.

Costovertebritis

This is the hallmark of spondyloarthropathy, and usually starts in the lower thoracic spine.

Complications

The most important spinal complications in ankylosing spondylitis include osteoporosis, fracture, instability, cauda equine syndrome and spinal stenosis.

Osteoporosis

Osteoporosis increases in prevalence directly with increased patient age, increased severity of spinal involvement, increased disease duration and peripheral arthritis. The vertebral marrow signal is usually increased on the T1 sequences as a result of the osteoporosis. The osteoporosis obviously increases the chances of vertebral

compression fractures, posterior element fractures, pseudoarthrosis and unstable fractures from relatively minor trauma.

Fractures

Fractures of the cervical spine can occur after a minor fall or injury to the head and neck. Typically the conventional radiographs show a chalk-stick type of break either through the disc or the vertebral body anteriorly and horizontally through the posterior fused elements. A common spinal location for fracture is the thoracolumbar and cervicothoracic and lastly the lumbosacral junction. By definition all three columns of the spine are involved in this type of fracture. There is a high risk of missing the fracture at the time of initial evaluation particularly if radiographic techniques are not optimal. A delayed diagnosis can lead to the development of a true pseudoarthrosis resulting in instability and cord injury. Increasingly it has been shown that conventional radiography is not sufficient in excluding a fracture complicating a fused spine in ankylosing spondylitis. Any ankylosing spondylitis patient suffering minor trauma who complains of pain should have advanced imaging preferably by CT, as this will show the full extent of the fracture in both the axial and the reconstructive sagittal and coronal images. If the patient has neurological deficit, MR is essential in assessing the status of the cord and in particular whether there is an epidural hematoma or disc/bone fragment compressing the cord.

Cauda Equina Syndrome

Cauda equina syndrome is a rare but specific complication following long-standing ankylosing spondylitis. It invariably occurs in a fused spine and is most common in the lumbar region. Dural ectasia producing leptomeningeal sacculations is common, resulting in erosions of primarily the posterior neural arch. This is best evaluated with CT or MRI. MR will show enlargement of the spinal canal with arachnoid diverticulae, erosion of the laminae and adherent nerve roots.

Spinal Stenosis

It is important that one remembers that the ligamentous ossification that takes place as a result of the chronic in-

flammatory reactive process can also involve the ligaments within the spinal canal, namely the longitudinal ligaments and the ligamentum flavum. As a result of this ossification there can be encroachment onto the contents, namely the cord and nerve roots. Neurological deficit in patients with ankylosing spondylitis could have a number of causes but C1-C2 subluxation, fracture, pseudoarthrosis, ligamentous ossification and cauda equine syndrome would tend to be the most common list that one needs to remember in directing imaging to the spine to assess the underlying reason for the neurological deficit.

Suggested Reading

1. Amrami KK (2012) Imaging of seronegative spondyloarthropathies. *Radiol Clin N Am* 50:841-854
2. Braun J, Bollow M, Eggens U et al (1994) Use of dynamic magnetic resonance imaging with fast imaging in the detection of early and advanced sacroiliitis in spondyloarthropathy patients. *Arthritis Rheum* 37:1039-1045
3. Dougados M, Baeten D (2011) Spondyloarthritis. *Lancet* 377:2127-2137
4. El-Khoury GY, Kathol MH, Brandser EA (1996) Seronegative spondyloarthropathies. *Radiol Clin North Am* 34:343
5. Fam A, Rubenstein J, Chin-Sang H et al (1985) Computed tomography in the diagnosis of early ankylosing spondylitis. *Arthritis Rheum* 28:930-937
6. Forrester D, Hollingsworth P, Dawkins RL (1983) Difficulties in the radiographic diagnosis of sacroiliitis. *Clin Rheum Dis* 9:323-332
7. Hollingsworth P, Cheah P, Dawkins RL et al (1983) Observer variation in grading sacroiliac radiographs in HLA-B27 positive individuals. *J Rheumatol* 10:247-254
8. Kurugoglu S, Kanberoglu K, Kanberoglu A et al (2002) MRI appearances of inflammatory vertebral osteitis in early ankylosing spondylitis. *Paediatr Radiol* 32:191-194
9. Toussiroit E (2010) Late-onset ankylosing spondylitis and spondyloarthritis: and update on clinical manifestations, differential diagnosis and pharmacological therapies. *Drugs Aging* 27:523-531
10. Van Der Linden S, Valkenburg H, Cats A (1984) Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum* 27:361-368
11. Weber U, Ostergaard M, Lambert RG et al (2011) The impact of MRI on the clinical management of inflammatory arthritides. *Skeletal Radiol* 40:1153-1173
12. Yu W, Feng F, Dion E et al (1998) Comparison of radiography, computed tomography and magnetic resonance imaging in the detection of sacroiliitis accompanying ankylosing spondylitis. *Skeletal Radiol* 27:311-320