REVIEW

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Spondyloarthropathies: Using presentation to make the diagnosis

ABSTRACT

Diagnosing the spondyloarthropathies—chronic inflammatory diseases of the spine and peripheral joints that share several distinctive features—is challenging and depends on careful evaluation of the history, physical examination, and radiographs. The recent use of tumor necrosis factor inhibitors is exciting and may represent true disease-modifying drugs for these conditions.

KEY POINTS

Common features of the spondyloathropathies are enthesitis of the axial and peripheral skeleton and variable involvement of the peripheral joints, gut, skin, eye, or aorta.

Human leukocyte antigen B27 is strongly associated with spondyloarthropathy but is not a diagnostic test.

Serologic tests for rheumatoid factor and antinuclear antibody are usually negative in patients with a spondyloarthropathy. The erythrocyte sedimentation rate and the C-reactive protein concentration are often elevated, but elevations do not always correlate with disease activity.

Tumor necrosis factor inhibitors have recently been approved for the treatment of spondyloarthropathy and may have disease-modifying effects. Clinical experience with these drugs in patients with spondyloarthropathies has been limited, but quite positive.

This paper discusses therapies that are experimental or are not approved by the US Food and Drug Administration for the use under discussion.

SPONDYLITIS IS EASY TO MISS and is often just assumed to be "back pain." Physicians should suspect a spondyloarthropathy in a young man or woman with morning stiffness lasting more than 30 minutes; or in a patient who has back pain and a history of uveitis, psoriasis, or inflammatory bowel disease; or in a patient with back pain that improves dramatically when the patient takes prednisone or a nonsteroidal anti-inflammatory drug (NSAID) for another reason.

Spondyloarthropathy is a family of arthritides that includes:

- Ankylosing spondylitis
- Reactive arthritis (including Reiter syndrome)
- Psoriatic arthritis
- Enteropathic spondyloarthropathy (ie, spondyloarthropathy associated with inflammatory bowel disease)
- Undifferentiated spondyloarthropathy (forms that fail to meet the clinical criteria for the other categories).[1]

The spondyloarthropathies are linked by association with the class 1 human leukocyte antigen (HLA)-B27 and by a common clinicopathologic lesion—enthesitis.

There is no serologic test to aid in the diagnosis. Rather, the diagnosis is made by analyzing a constellation of factors, such as axial and peripheral joint and skeletal involvement, associated clinical features, and genetic predisposing factors.[2]

Treatment has been focused on the relief of symptoms with drugs such as nonsteroidal anti-inflammatory drugs. The new tumor necrosis factor inhibitors may have a role in modifying the course of this family of conditions, but experience with these drugs is limited.

TABLE 1

Demographic features of the spondyloarthropathies

	GENERAL PREVALENCE	RELATIVE PREVALENCE*	PERCENTAGE OF MALE PATIENTS	MEAN AGE (YEARS) AT DIAGNOSIS	POSITIVE FOR B27 ANTIGEN
Ankylosing spondylitis	0.86%	42%	75%	41	86%
Reactive arthritis	0.1%	17%	75%	33	69%
Psoriatic arthritis	0.29%	10%	43%	47	20%-34%
Enteropathic	NA	4%	67%	38	50%-75%
Undifferentiated	0.67%	27%	31%	53	18%

*Based on the European Spondyloarthropathy Study Group data from seven rheumatology centers, including 403 patients diagnosed with spondyloarthropathy.

In this article, we review the clinical presentation of the spondyloarthropathies to help guide the clinician through diagnosis and treatment.

EPIDEMIOLOGY

An epidemiologic assessment of blood donors in Berlin, Germany,[3] found that 1.9% had a spondyloarthropathy: 0.86% had ankylosing spondylitis, 0.67% had undifferentiated spondyloarthropathy, and 0.29% had psoriatic arthritis. Reactive arthritis and enteropathic spondylitis were much less common.[3]

The prevalence of spondyloarthropathy, particularly of ankylosing spondylitis, correlates most strongly with the prevalence of HLA-B27 in the general population. The percentage of spondyloarthropathy patients with this gene varies from about 90% in those with ankylosing spondylitis to 20% in those with psoriatic arthritis or undifferentiated spondyloarthropathy (TABLE 1).[4–9] Ankylosing spondylitis and reactive arthritis are more common in men, but are likely underdiagnosed in women. The mean age at diagnosis is generally in the 30s and 40s. Most people with the HLA-B27 gene do not develop ankylosing spondylitis.

TABLE 1[3–11] provides the key demographic characteristics of the spondyloarthropathies.

THEORIES OF PATHOGENESIS

Genetic, immunologic, and environmental factors appear to work in concert in the pathogenesis of the spondyloarthropathies, but the exact cause and pathogenesis remain unclear.

The role of the human histocompatibility complex

The spondyloarthropathies are variably associated with the HLA class I antigen B27.[3] The histocompatibility or HLA complex is responsible for antigen recognition, allowing the distinction between self and nonself. In humans, the HLA complex is located on chromosome 6 and is made up of genes that code for HLAs. HLA class I genes code for HLA-A, HLA-B, and HLA-C molecules, which are expressed on all nucleated cells. HLA class II genes code for HLA-DR, HLA-DQ, and HLA-DP molecules, found on antigen-presenting cells such as macrophages and dendritic cells.

An important biologic role of the HLA molecules is to present antigenic peptides in a manner that enables appropriate T-cell receptors to engage them while simultaneously discriminating self from nonself, leading to T-cell activation. HLA class I molecules generally present antigen to CD8-positive T cells, whereas HLA class II molecules generally present antigen to CD4-positive T cells.

Only a minority of people with the B27 gene develop spondylitis. While 90% of Caucasian patients with ankylosing spondylitis are B27-positive, far fewer African Americans or Asians with this disease have this antigen.

Genetic immunologic, and environmental factors appear to work together in spondyloarthropathies

Molecular mimicry and an environmental stimulus

The shared amino acid sequence between the antigen-binding region of HLA B*2705 and nitrogenase from *Klebsiella pneumoniae* supports molecular mimicry as a possible mechanism for the induction of spondyloarthropathy in genetically susceptible hosts by an environmental stimulus, such as bacteria in the gastrointestinal tract.[12] Another possible mechanism is presentation of an arthritogenic peptide from enteric bacteria by specific HLA molecules. Many patients with ankylosing spondylitis have subclinical gastrointestinal tract inflammation and elevated serum immunoglobulin A antibodies directed against *Klebsiella*. The bacteria may invade the gastrointestinal tract of a genetically susceptible host, leading to chronic inflammation and increased permeability. Over time, bacterial antigens containing arthritogenic peptides enter the blood stream. Bacterial antigens are thought to play a role in the pathogenesis of reactive arthritis.[13] Further studies are needed to establish their exact role in the pathogenesis of reactive arthritis and related arthritides. Experimental work with transgenic mice and rats transfected with human HLA-B27 and beta-2-microglobulin has shown that certain strains develop a multisystemic illness resembling spondyloarthropathy, whereas identical animals raised in a germ-free environment remain healthy.[14,15]

CLASSIFICATION AND DIAGNOSIS

The system most commonly used to classify spondyloarthropathies for diagnostic purposes[10] is the European Spondyloarthropathy Study Group (ESSG) criteria,[10] which have a sensitivity of 83.5% and a specificity of 95.2%. Diagnosis is based on the presence of one of two major criteria (inflammatory spinal pain or synovitis) plus one or more of the following:

- Positive family history of ankylosing spondylitis, psoriasis, acute uveitis, reactive arthritis, or inflammatory bowel disease (all linked to the presence of B27 and spondylitis)
- Psoriasis
- Inflammatory bowel disease
- Urethritis, cervicitis, or acute diarrhea less than 1 month before arthritis
- Alternating buttock pain
- Enthesitis
- Sacroiliitis.

According to the Amor criteria,[16] which are less commonly used, the diagnosis is based on a total score derived from consideration of 12 weighted criteria, which include history, clinical presentation, radiologic findings, genetic background, and response to treatment. This method is less convenient than the ESSG criteria. Its rates of sensitivity (90.8%) and specificity (96.2%) are statistically comparable to those of the ESSG method.[17]

TABLE 2

Common features of the spondyloarthropathies

Inflammatory back pain
Morning stiffness that is reduced with activity

Peripheral arthritis
Typically asymmetric, occurring predominantly in the lower limbs

Enthesitis
Achilles tendon insertion
Plantar fascia insertion on calcaneus
Patella, superior and inferior aspects
Tibial tuberosity
Metatarsal heads
Base of fifth metatarsal joint
Iliac spine, iliac crest
Ischial tuberosity
Tarsal region
Greater trochanter
Lateral epicondyle
Distal scapula
Distal ulna

Dactylitis

Radiographic evidence of reactive proliferation of new bone at the site of enthesitis

Radiographic sacroiliitis

Characteristic extra-articular features (eg, anterior uveitis)

Significant family history

Presence of human leukocyte antigen B27

The ESSG criteria are commonly used to facilitate the diagnosis

TABLE 3

Characteristics of spine and eye disease in the spondyloarthropathies

	SACROILIITIS	SPONDYLITIS	SYNDESMOPHYTES	UVEITIS
Ankylosing spondylitis	Symmetric	Continuous, ascending	Delicate, marginal	Acute, unilateral, recurrent
Reactive arthritis	Asymmetric	Discontinuous*	Bulky, nonmarginal	Acute, unilateral, recurrent
Psoriatic arthritis	Asymmetric	Discontinuous	Bulky, nonmarginal	Chronic, bilateral
Enteropathic spondyloarthropathy	Symmetric	Continuous, ascending	Delicate, marginal	Chronic, bilateral
Undifferentiated spondyloarthropathy	None	Minimal	Occasional	Uncommon, usually acute unilateral

*Areas of spinal involvement are not continuous or contiguous with areas of normal-appearing spine between areas of spondylitis.

These general diagnostic criteria are useful for the diagnosis of spondyloarthropathies, including atypical, undifferentiated forms.

GENERAL FEATURES OF ALL SPONDYLOARTHROPATHIES

Elevated ESR, and CRP are common, but often not correlated with disease activity

The features shared by all spondyloarthropathies (TABLE 2, TABLE 3) are inflammatory back pain, peripheral arthritis, enthesitis, dactylitis, and uveitis. But even though all types of spondyloarthropathy can exhibit these features, the pattern of these features helps define the distinct form of spondyloarthropathy.

For example, symmetric sacroiliitis, gradually ascending spondylitis, and delicate, marginal syndesmophytes (intervertebral bony bridges) are seen more commonly in ankylosing spondylitis, whereas asymmetric sacroiliitis, discontinuous spondylitis, and bulky, nonmarginal syndesmophytes are more common in reactive arthritis and psoriatic arthritis. Sacroiliac and lumbar spine disease are not typically found in rheumatoid arthritis.

Peripheral arthritis

Inflammatory arthritis of the peripheral joints can occur in patients with spondyloarthropathy. However, the arthritis is usually asymmetric, distinguishing it from the typical symmetric polyarthritis of rheumatoid arthritis and other connective tissue diseases.

Enthesitis and dactylitis

Enthesitis is inflammation at the site of attachment of ligaments, tendons, and other structures onto bone. It is a common clinical feature of spondyloarthropathy and is found most often in the heel or knee (TABLE 2). It may occasionally be seen in rheumatoid arthritis, systemic lupus erythematosus, or sarcoidosis but is rare in other diseases.

Dactylitis, or "sausage digit," is less common than enthesitis and is found more often in reactive arthritis and psoriatic arthritis than in the other spondyloarthropathies. It is occasionally seen in sarcoidosis but is rare in other rheumatic diseases.

Uveitis

Uveitis in ankylosing spondylitis and reactive arthritis is usually acute, unilateral, and recurrent and rarely involves posterior elements. In contrast, uveitis in patients with psoriatic arthritis and spondylopathy associated with inflammatory bowel disease is often chronic and bilateral and more often involves posterior elements.

Laboratory features

Patients with a spondyloarthropathy are often found to have the B27 antigen, but B27 antigen status lacks specificity and therefore is not itself diagnostic. Serologic tests for rheumatoid factor and antinuclear antibody are usually negative in patients with a spondy-

TABLE 4

Inflammatory vs degenerative spinal disease: A comparison of features

FEATURE	INFLAMMATORY SPINAL DISEASE	DEGENERATIVE SPINAL DISEASE
Age at onset	Younger than age 40	From age 20 to age 90
Type of onset	Insidious	Variable
Duration	Longer than 3 months	Variable
Morning stiffness	Longer than 30 minutes	Less than 30 minutes
Effect of physical activity	Improves symptoms	Worsens symptoms
Radiation of pain	Diffuse	Radicular
Multisystem disease	Yes	No
Family history	Often	Variable

loarthropathy. The erythrocyte sedimentation rate (ESR) and the C-reactive protein (CRP) concentration are often elevated, but elevations may not correlate with disease activity.

ANKYLOSING SPONDYLITIS

Axial skeletal involvement

Back pain is an extremely common complaint in medical practice, occurring in up to 80% of the general population, and the pain is most commonly due to a mechanical problem.

In ankylosing spondylitis, however, the back pain is due to inflammation (TABLE 4).[18] The patient may first feel pain from the sacroiliac joints deep in the gluteal regions. This pain is insidious in onset. It is dull and difficult to localize and is often worse on awakening.

The Schober test measures spinal mobility with bending, although a positive test is not specific for ankylosing spondylitis. Spinal mobility with bending can be seen to improve with treatment.

Buttock pain is typically either unilateral or alternating from side to side. With subsequent involvement of the thoracic spine, including costovertebral, costosternal, and manubriosternal joints, patients may experience chest pain that is accentuated by coughing or sneezing and is sometimes characterized as "pleuritic." Mild to moderate reduction of chest expansion may occur.

Peripheral skeletal involvement

Tenderness may occur over sites of enthesitis, including costosternal junctions, spinous processes, iliac crests, greater trochanters, ischial tuberosities, tibial tuberosities, or heels at the insertion of the Achilles tendon or plantar fascia.

Hips and shoulders are the most frequently involved peripheral joints in ankylosing spondylitis. Asymmetric peripheral arthritis occurs in 35% of patients, whereas enthesitis occurs in 20%. Hip and ankle pain are more common initial presentations if the disease starts in childhood. Temporomandibular joint involvement occurs in about 10% of patients.

Back pain in early ankylosing spondylitis is not mechanical but due to inflammation

Extra-articular manifestations

Anterior uveitis or iridocyclitis (inflammation of the iris and ciliary body) is the most common extra-articular manifestation of ankylosing spondylitis, occurring in 25% to 30% of patients at some time during the course of the disease. Anterior uveitis in the absence of spondylitis is also associated with the B27 antigen.

Other extra-articular manifestations are uncommon and usually occur late in the course of the disease:

Cardiac involvement may include ascending aortitis, aortic insufficiency, conduction abnormalities, cardiomegaly, and pericarditis.

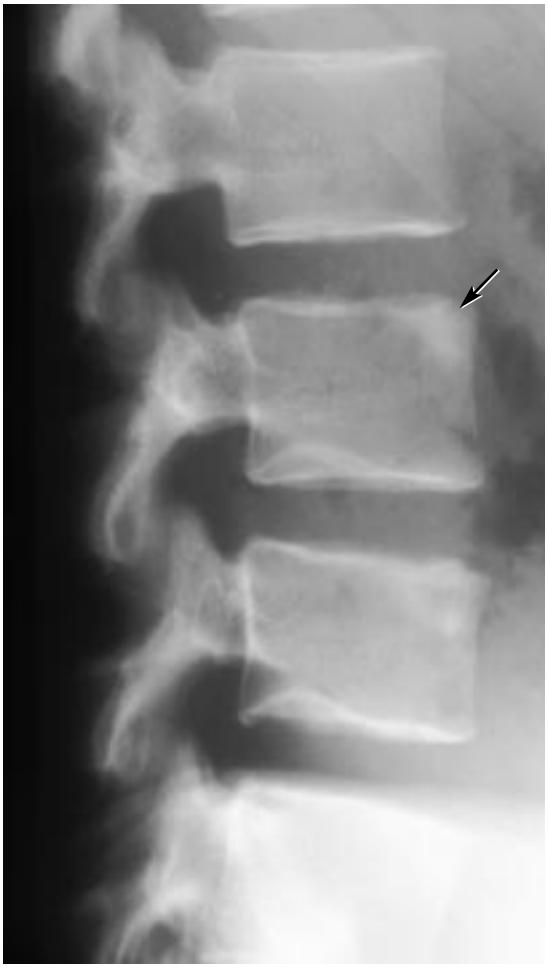

FIGURE 1. Radiograph of the lumbar spine in a patient with ankylosing spondylitis showing reactive sclerosis and erosions at the corners of the vertebral bodies, or "shiny corners"(arrow).

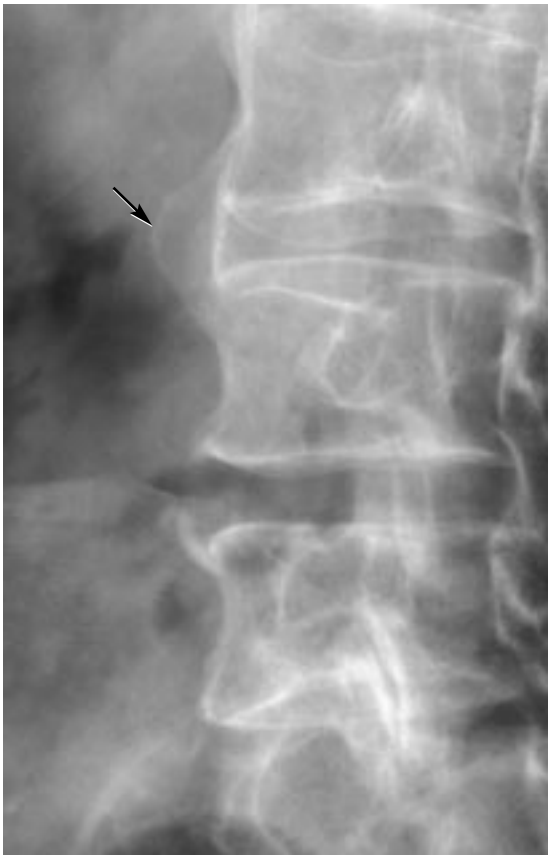

FIGURE 2. Radiograph of the lumbar spine in a patient with ankylosing spondylitis showing syndesmophyte formation including bridging (arrow) due to ossification of the annulus fibrosus.

Key feature of ankylosing spondylitis: inflammatory-pattern back pain with stiffness and a family history of the disease

Lung involvement is characterized by slowly progressive fibrosis of the upper lobes that appears, on average, 2 decades after the onset of ankylosing spondylitis. The lesions may cavitate and be colonized by *Aspergillus* species.

Neurologic complications can be caused by fracture, instability, or compression of the spine. Cauda equina syndrome is a rare but serious complication of long-standing ankylosing spondylitis.

Diagnostic considerations

Clinical manifestations of ankylosing spondylitis usually begin in late adolescence or early adulthood. In rare cases, they begin after age 40 or in childhood. Two features of the history are critically important: inflammatory-pattern back pain with stiffness and a family history of ankylosing spondylitis.

The diagnosis is usually established by radiographic evidence of bilateral sacroiliitis,[19,20] in addition to a clinical feature such as inflammatory back pain, limitation of lumbar spine motion, or decreased chest expansion. Testing for the B27 antigen has no value in routine screening and should not be regarded as diagnostic or confirmatory in patients with back pain.[21]

Laboratory and radiologic evaluation

An elevated ESR or CRP is seen in up to 75% of patients with ankylosing spondylitis, but this may lack correlation with clinical disease

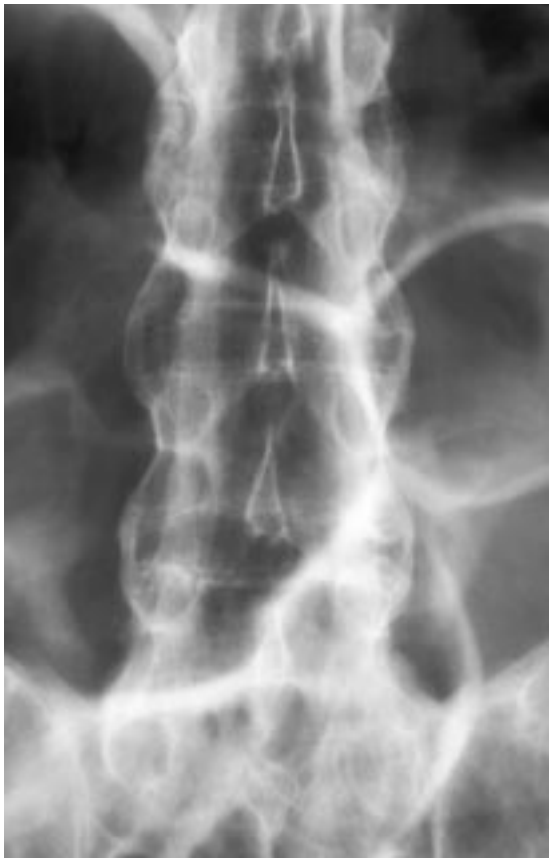

FIGURE 3. Radiograph of the lumbar spine in a patient with late-stage ankylosing spondylitis showing extensive syndesmophyte formation with bridging ossification of the annulus fibrosus ("bamboo spine").

Gonococcal arthritis and inflammatory bowel disease can mimic reactive arthritis

activity. A mild normochromic, normocytic anemia is present in 15% of patients.

Radiographic changes of the sacroiliac joints are usually symmetric and consist of blurring of the subchondral bone plate, followed by erosions and sclerosis of the adjacent bone.

Conventional plain radiography of the pelvis is a good screening tool for evaluation of sacroiliac joints in patients with inflammatory back pain. In the early stages of the evolution of syndesmophytes, there is inflammation of the superficial layers of the annulus fibrosus with subsequent reactive sclerosis and erosion of the adjacent corners of the vertebral bodies (called "shiny corners") (FIGURE 1). This combination of destructive osteitis and repair leads to "squaring" of the vertebral bodies. The inflammatory process is associated with gradual ossification of the annulus fibrosus and eventual "bridging" between vertebrae by syndesmophytes (FIGURE 2). This may ultimately result in a virtually complete fusion of the vertebral column, resulting in the "bamboo spine" (FIGURE 3). Bony erosion and osteitis at sites of osseous attachment of tendons and ligaments are common, particularly at the calcaneus, ischial tuberosities, iliac crest, femoral trochanters, and spinous processes of vertebrae.

REACTIVE ARTHRITIS AND REITER SYNDROME

Reactive arthritis is an acute spondyloarthropathy that usually follows a urogenital or enteric infection, often in patients positive for the HLA-B27 antigen, although this is less frequent than in ankylosing spondylitis. Reiter syndrome[22,23]—arthritis, urethritis/cervicitis, and conjunctivitis—is now considered a subset of reactive arthritis.

Diseases such as gonococcal arthritis and inflammatory bowel disease can mimic reactive arthritis and should be excluded before making the diagnosis of reactive arthritis.

Articular manifestations

The most distinctive musculoskeletal manifestation of reactive arthritis is enthesitis, occurring in 70% of patients, most commonly in the heel or knee regions.

In reactive arthritis, the arthritis typically appears within 1 to 4 weeks of infectious exposure. Constitutional symptoms are usually mild, and fever, if present, is low-grade. Joint stiffness and myalgias are prominent early symptoms. The pattern of arthritis is typically an acute, additive, asymmetric oligoarthritis mainly involving the lower extremities.

Axial skeletal involvement including sacroiliitis and spondylitis occurs clinically in about 50% of patients, although radiographic changes are seen in only 20% initially. Occasionally, the upper extremities are involved in an asymmetric fashion, especially the hands and wrists. The knee can become markedly swollen, with inflammatory synovial fluid, popliteal cyst dissection, and rupture.

Exuberant calcaneal spurs may eventually develop due to ossification of the tendinous insertions. Dactylitis or sausage digits may occur due to flexor tenosynovitis in the fingers or toes.

Extra-articular manifestations

Urethritis may be a principal feature of reactive arthritis, but genitourinary manifestations can also include cervicitis, salpingitis, vulvovaginitis, aseptic pyuria, and prostatitis. A sterile form of urethritis can be seen after *Salmonella* and *Shigella* infection, as well as after urogenital or chlamydial infection.

The precipitating episode of diarrhea is often mild, but occasionally it may be bloody and prolonged. Patients with *Yersinia* enteritis often have mild, recurrent abdominal complaints.

Small, shallow, painless ulcers of the glans penis and urethral meatus (balanitis circinata) have been described and may precede symptoms of arthritis. In uncircumcised patients, the lesions are moist and are asymptomatic unless secondarily infected. The foreskin has to be retracted during the physical examination to detect these lesions. On the circumcised penis, the lesions harden to a crust, which may scar and cause pain.

Keratoderma blennorrhagica is a hyperkeratotic skin lesion that is seen in 12% to 14% of patients. It begins as clear vesicles on erythematous bases and progresses to macules, papules, and nodules. The lesions are often found on the soles of the feet, but they may also be found on the toes, palms, scrotum, penis, trunk, and scalp. The lesions are indistinguishable clinically and microscopically from pustular psoriasis. Onycholysis may occur.

Superficial oral ulcers are an early and transient feature of the disease. Erythema nodosum is a feature of *Yersinia* enteritis, and can mimic inflammatory bowel disease.

Conjunctivitis is the most common ocular complication of reactive arthritis. It occurs in the majority of patients with *Shigella* infections and is often the initial symptom. It also occurs after *Salmonella* and *Campylobacter* infections. About 35% of patients with postvenereal reactive arthritis develop conjunctivitis. Uveitis may occur as an independent, asynchronous event due to the shared genetic susceptibility related to the B27 antigen.

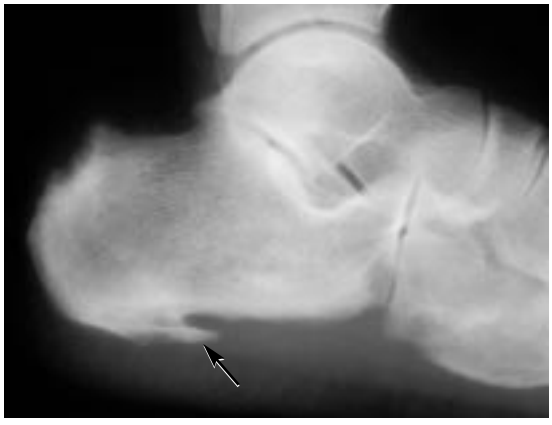

FIGURE 4. Radiograph of the heel in a patient with Reiter syndrome, showing lesions secondary to enthesitis including erosions (insertion of the Achilles tendon on the calcaneus) and periosteal new bone formation (insertion of the plantar fascia on the calcaneus) (arrow).

Cardiac complications are reported as late sequelae in 10% of patients with severe, long-standing disease including conduction abnormalities and aortic regurgitation. Conduction disturbances range from a prolonged PR interval to complete heart block.[24]

Laboratory evaluation

The infection triggering the reactive arthritis should be sought and treated as warranted. Often, however, the local infection has resolved by the time features of reactive arthritis have developed. Prolonged antibiotic treatment courses have not been shown to reliably influence the course of the arthritis.

Often, the infection has resolved by the time reactive arthritis develops

Radiographic evaluation

The characteristic radiographic feature is not joint erosion, as in rheumatoid arthritis, but reactive new bone formation at sites of enthesitis (FIGURE 4). The presence of bony proliferation as seen in reactive arthritis, psoriatic arthritis, and ankylosing spondylitis is the most helpful radiographic feature in distinguishing these diseases from rheumatoid arthritis. Linear periostitis along the metacarpal, metatarsal, and phalangeal shafts, and exuberant periosteal spurs with indistinct margins can be seen along the sites of tendi-

nous insertion onto bone.

In the spine, asymmetric, paravertebral, comma-shaped ossification is a characteristic finding on plain radiography in reactive arthritis and psoriatic arthritis. It typically involves the lower three thoracic and upper three lumbar vertebrae. In contrast to ankylosing spondylitis, squaring of the vertebrae is uncommon. Plain radiographs of the spine are abnormal in up to 70% of cases of chronic reactive arthritis.

PSORIATIC ARTHRITIS

Psoriatic arthritis is defined as inflammatory arthritis associated with psoriasis and a negative rheumatoid factor.

Articular manifestations

Five general patterns of joint involvement have been described.[25]

- Asymmetric oligoarthritis: most joints may be involved; small joints of hands and feet are often involved, including the distal interphalangeal joints.
- Symmetric polyarthritis indistinguishable from rheumatoid arthritis: similar to that seen in rheumatoid arthritis, but with a negative rheumatoid factor. Patients with psoriasis, symmetric polyarthritis, and positive rheumatoid factor are considered to have rheumatoid arthritis and concomitant psoriasis.
- Arthritis of the distal interphalangeal joints: this form is commonly associated with nail changes. Inflammation of these joints is not seen in rheumatoid arthritis.
- Destructive arthritis (arthritis mutilans): severe deforming arthritis of small joints of the hands and feet, with osteolysis; patients may have constitutional symptoms, usually associated with severe skin disease and sacroiliitis.
- Spondylitis: may occur alone or with other forms of psoriatic arthritis and is often asymptomatic; sacroiliitis is usually asymmetric, and syndesmophytes are usually bulky, nonmarginal, and discontinuous, as in reactive arthritis.

Acute peripheral psoriatic arthritis can mimic gout

Other musculoskeletal features of psoriatic arthritis include dactylitis, tenosynovitis, and enthesitis. Dactylitis occurs in more than 30% of patients and is characterized by a diffuse swelling of the entire digit along with arthritis of the distal interphalangeal, proximal interphalangeal, and metacarpophalangeal or metatarsophalangeal joints. Dactylitis is not seen in rheumatoid arthritis.

Extra-articular manifestations

The diagnosis of psoriatic arthritis cannot be made with certainty in the absence of psoriasis. A physical examination for hidden psoriatic lesions, particularly in the ears, the hairline, the umbilical area, the gluteal crease, and the nails is mandatory. Nail changes such as pitting, ridging, and onycholysis are often seen. Onset of arthritis occurs before skin disease in up to 20% of patients. Uveitis has been reported in 18% of patients.[7]

Laboratory and radiographic evaluation

Low titers of rheumatoid factor have been detected in 5% to 16% of patients, and antinuclear autoantibodies have been detected in 2% to 16% of the patients with psoriatic arthritis.[8,26,27] If high titers of rheumatoid factor are present in the setting of symmetric polyarthritis, the patient is considered to have rheumatoid arthritis and concomitant psoriasis.

Characteristic radiographic features include asymmetric distribution, involvement of distal interphalangeal joints, sacroiliitis, spondylitis, bone erosions and periosteal new bone formation, bony ankylosis, and resorption of the distal phalanges. The typical late change in the peripheral joint is the "pencil-in-cup" erosion marked by lysis of the distal end of the proximal phalanx, with remodeling of the proximal end of the more distal phalanx. Involvement of temporomandibular, sternoclavicular, and manubriosternal joints is common. The presence of periosteal reaction is also characteristic of enthesitis seen in this condition. Sacroiliitis tends to be asymmetric. In the spine, as in reactive arthritis, bulky, nonmarginal syndesmophytes are seen more frequently than marginal syndesmophytes.

ENTEROPATHIC SPONDYLOARTHROPATHY

Articular manifestations

Between 10% and 20% of patients with inflammatory bowel disease develop arthritis,

slightly more often in Crohn disease than in ulcerative colitis. This enteropathic arthritis is usually nondestructive and reversible.

Enteric spondyloarthropathy can occur in one of three patterns. One is a peripheral asymmetric arthritis with fewer than five joints involved. Second is a peripheral symmetric polyarthritis with five or more joints involved. And the third pattern is characterized by spinal involvement with sacroiliitis and spondylitis, sometimes with peripheral joint involvement.[28,29]

The peripheral arthritis may precede the diagnosis of inflammatory bowel disease and, once established, often parallels the activity of the inflammatory bowel disease. Spondylitis rarely occurs prior to the diagnosis of inflammatory bowel disease and does not correlate with the disease activity of the underlying bowel disease.

Extra-articular manifestations

Clubbing of fingers, uveitis, erythema nodosum, and pyoderma gangrenosum are also observed in inflammatory bowel disease, with a higher frequency in Crohn disease.[4] Subclinical inflammatory lesions in the gut are common, as observed on colonoscopic mucosal biopsy studies in patients with spondyloarthropathy but no gastrointestinal symptoms. Follow-up studies of such patients indicate that 6% develop inflammatory bowel disease and, of those with inflammatory gut lesions, 15% to 25% develop clinical Crohn disease.[30] This suggests that patients with subclinical inflammatory bowel disease can present with extraintestinal manifestations, making diagnosis more challenging.

UNDIFFERENTIATED SPONDYLOARTHROPATHY

"Undifferentiated spondyloarthropathy" represents a working diagnosis for patients who have manifestations consistent with a spondyloarthropathy but who do not meet the criteria for its well-defined forms. At present, it is unclear if these patients have an early, incomplete form of a defined spondyloarthropathy.

A good history and physical examination documenting inflammatory back pain, enthesitis, or dactylitis (FIGURE 5) should raise the suspicion of a spondyloarthropathy. Often, the passage of time with repeated history and examinations will clarify the nature of any underlying disease.

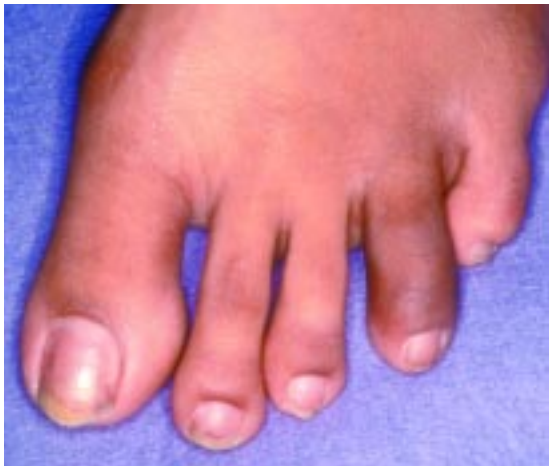

FIGURE 5. Dactylitis involving the left fourth toe in a patient with undifferentiated spondyloarthropathy.

TREATMENT OF SPONDYLOARTHROPATHIES

It is difficult to test treatments for the spondyloarthropathies because the disease—especially the spinal involvement—progresses slowly. In the absence of specific treatments, the general goals of therapy are to control symptoms of morning stiffness and pain, to slow or stop disease progression, and to help the patient maintain erect posture and functional ability.

10%–20% of patients with inflammatory bowel disease develop arthritis

Drug therapy

NSAIDs have been the mainstay of therapy, but they have not been shown to slow or stop disease progression. Cyclooxygenase-2 inhibitors are likely effective and have an improved gastric safety profile compared with nonselective NSAIDs. Nonselective NSAIDs are often avoided in spondyloarthropathy associated with inflammatory bowel disease. NSAIDs are often very beneficial in patients with undifferentiated spondyloarthropathy.[31,32]

If patients do not response to NSAIDs, one of the following second-line therapies should be considered.

Sulfasalazine

Sulfasalazine has been shown to be effective for controlling inflammatory symptoms of spondyloarthropathy over the short term, especially peripheral musculoskeletal involvement.[33–35] Sulfasalazine was effective in reducing synovitis in patients with peripheral polyarticular involvement but had no effect on axial involvement.[36] Although sulfasalazine has disease-modifying activity in rheumatoid arthritis, this has not been documented for spondyloarthropathy.[37]

Methotrexate

Methotrexate has been shown to be effective in the treatment of the articular and skin manifestations of psoriatic arthritis.[38] In small studies of patients with ankylosing spondylitis, there was apparent benefit for peripheral but not axial involvement.[39–42]

Corticosteroids

Oral corticosteroids are occasionally used in patients with a spondyloarthropathy who have severe polyarticular symptoms unresponsive to other treatments, especially patients with psoriatic arthritis. Intra-articular injections are used for monoarticular or oligoarticular flares. In our experience, spondyloarthropathy does not respond as well to oral or injected corticosteroids as does rheumatoid arthritis. However, some patients' axial or peripheral arthritis may respond dramatically to a therapeutic course of corticosteroids.

Tumor necrosis factor inhibitors

Infliximab has been used in the treatment of spondyloarthropathies, including ankylosing spondylitis[43,44] and psoriatic arthritis,[45,46] in relatively small studies that showed benefit. Etanercept has been shown to effectively control the articular and cutaneous manifestations of psoriatic arthritis[47,48] and can inhibit radiographic progression as well.[49] A recent double-blind, placebo-controlled trial showed etanercept to be effective in treating the musculoskeletal symptoms of ankylosing spondylitis.[50] Etanercept recently was approved by the US Food and Drug Administration for the treatment of active ankylosing spondylitis.

Other therapies

Physical therapy, especially extension exercises for the spine, is believed to help the patient maintain erect posture. Orthopedic surgery—including total joint arthroplasty of the hips and knees and, in rare cases, corrective spinal surgery—may be beneficial. However, heterotopic bone formation may occur after total joint arthroplasty, especially at the hip joint, and prophylactic treatment should be considered.

Studies of TNF inhibitors are small but encouraging

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