Enthesopathies, Inflammatory Spondyloarthropathies and Bone Scintigraphy

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Entheses are the site of bony attachments of ligaments and tendons. Inflammatory changes at these sites (enthesopathy) may be the first or only sign of this disease and the leading manifestation of disease in patients with inflammatory spondyloarthropathies (*1*). It is most commonly found at the insertions of the achilles tendon and the plantar fascia but may occur in other sites such as spine and pelvis, femoral trochanter, humeral tuberosity, tibial tuberosity, patella and olecranon. Awareness of the patterns of enthesopathy findings on bone scans may help in the early diagnosis of systemic inflammatory spondyloarthropathy. Increased uptake of ^{99m}Tc-methylene diphosphonate (MDP) at the site of bony attachments of tendons and ligaments combined with increased uptake at peripheral or axial joints in a complementary clinical setting are characteristic of different types of inflammatory spondyloarthropathies. The following cases illustrate the bone-scan findings of enthesopathy in patients with inflammatory spodyloarthropathy.

CASE REPORT

Patient 1

An 18-yr-old man with a 6-mo persistent arthritis of the right ankle and foot was admitted. There was a history of dysuria and transient conjunctivitis a few months before admission. The examinations including hematologic, chemical, rheumatoid factor, antinuclear factor (ANF), serology for chlamydia, ureaplasma urealyticum, Venereal Disease Research Laboratories and human immunodeficiency virus were all normal. An elevated erythrocyte sedimentation rate (ESR) of 33 mm/hr was noted. Conventional radiographs of the chest, pelvis, ankles and feet and CT of the ankles were normal. The bone scan showed increased blood pool (Fig. 1) in several tarsal and metatarsal joints in both feet and at the insertion of the achilles tendon and plantar fascia in the calcaneus. The delayed scan showed increased focal abnormal uptake in several joints of the ankle and forefoot due to synovial inflammation and increased abnormal uptake suggesting enthesopathy at the attachments of the achilles tendon and plantar fascia in both feet (Fig. 2). A diagnosis of reactive arthritis was suggested by the finding of multiple joint involvement and the characteristic appearance of the calcaneus enthesopathy on the scan. The patient was treated with a nonsteroidal anti-inflammatory drug (NSAID) and minocycline for 6 mo with complete remission of the disease.

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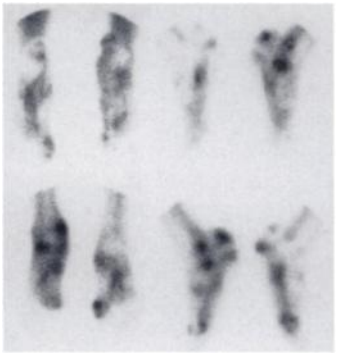

FIGURE 1. Blood-pool images in plantar (top left), lateral (top right), anterior (bottom left) and medial (bottom right) views show an increased blood pool in several tarsal and metatarsal joints in both feet and at the calcaneus.

Patient 2

A 36-yr-old woman with polyarthritis of the hands, wrists and knees for 2 yr, seronegative and not improved by NSAID was admitted to the rheumatology department for evaluation. The ESR was elevated 60 mm/hr, ANF, rheumatoid factor and serology for hepatitis B and C were negative. Conventional radiographs of the hands, feet, knees, pelvis and chest were normal. The bone scan showed increased abnormal focal uptake in several metatarsal phalangeal joints due to synovial inflammation and increased abnormal focal uptake at the calcaneus due to enthesopathy at the insertion site of the achilles tendon (Fig. 3). In the upper limb, there is increased uptake in several metacarpophalangeal and wrist joints due to synovial inflammation and increased abnormal focal uptake in both olecranon due to enthesopathy at the insertion of the triceps tendon (Fig. 4). The diagnosis of inflammatory spondyloarthropathy was suggested by the characteristic appearance of the enthesopathy combined with joint involvement by the scan. Reactive arthritis related to human leucocyte antigen B27 was later confirmed. Treatment with sulfasalazine was initiated with partial response.

DISCUSSION

Entheses are the sites of tendon, ligament and articular capsule insertion to bone (*1*). Enthesopathy is a disease occurring at these sites, which may occur alone (idiopathic) or accompanying other disorders such as inflammatory, degenerative, metabolic or traumatic conditions (*1–3*). The sites most

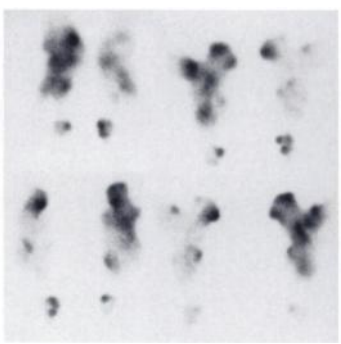

FIGURE 2. Delayed images in the anterior (top left), medial (top right), plantar (bottom left) and lateral (bottom right) views show increased uptake in several joints of the ankle and forefoot due to synovial inflammation and increased uptake suggestive of achilles tendinitis and plantar fasciitis in both calcaneus. There were no other joints or entheses with abnormal uptake on the bone scan.

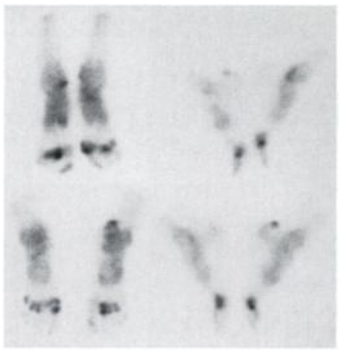

FIGURE 3. Delayed images in the anterior (top left), medial (top right), plantar (bottom left) and lateral (bottom right) views show increased uptake in several metatarsal phalangeal joints due to synovial inflammation and at the attachment of the right achilles tendon to the calcaneus due to enthesopathy.

frequently involved are the pelvis, femoral trochanter, humeral tuberosity, patella, olecranon, calcaneus and vertebrae. Any enthesis may be affected (*1*). Enthesopathy is one of the features characterizing patients with inflammatory spondyloarthropathy (*3–5*). The diagnosis is usually based on clinical symptoms such as the presence of pain or focal tenderness at insertions of ligaments or tendons. The typical osseous erosion with proliferation at an entheses shown by radiographs are late findings of enthesopathy in patients with inflammatory spondyloarthropathy (*3*). More objective means to assess the presence and nature of enthesopathy are needed. Computerized tomography and MRI are the techniques commonly used to evaluate abnormalities of tendons and ligaments. These methods are useful in detecting morphological changes accompanying degeneration, inflammation, calcification, disruption and bone avulsion (*3,4,6*).

Bone scintigraphy plays a role in the evaluation of inflammatory spondyloarthropathy. It is a sensitive test that detects areas of abnormal bone turnover and reflects the activity of a disease process, the inflammatory focus, rather than its morphological consequences. Also, the ability to perform a whole-body scan yields investigation of multiple sites affected by a generalized disease process. The distribution of the joints involved combined with enthesopathy demonstrated on bone scintigraphy, in the appropriate clinical setting, can suggest a specific inflammatory spondyloarthropathy diagnosis.

Inflammatory spondyloarthropathies comprise a group of multisystem inflammatory disorders sharing similar clinical, radiographic, pathological and genetic characteristics (*3–7*). They include Ankylosing spondylitis (AS), psoriatic arthritis (PA), reactive arthritis (Reiter's syndrome) and arthritis associated with inflammatory bowel disease. Those that cannot be classified are referred to as undifferentiated spondyloarthropathy (*6*). Inflammation of the cartilaginous joints and entheses in conjunction with involvement of the synovial joints shows a characteristic distribution for each one of the disorders (*3*).

Ankylosing spondylitis changes are present usually in the axial skeleton affecting the synovial and cartilaginous joints and entheses of the sacroiliac joints and spine. Involvement of the

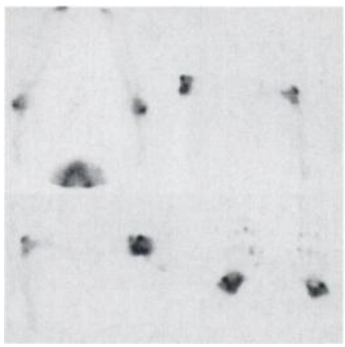

FIGURE 4. Delayed images of the elbows and hands show increased uptake in several metacarpal phalangeal, interphalangeal and wrist joints due to synovial inflammation and increased uptake in both olecranon due to enthesopathy.

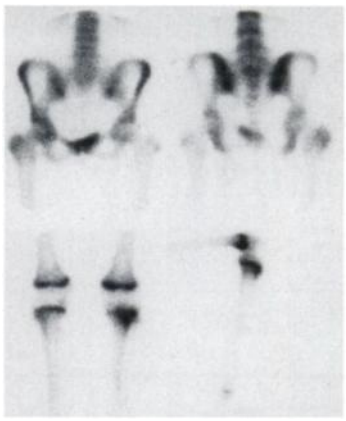

FIGURE 5. Delayed bone scan on a 15-yr-old girl with ankylosing spondylitis shows bilateral increased uptake at the lower sacroiliac joint and at the right greater trochanter and left tibial tuberosity due to enthesopathy.

sacroiliac joint is mandatory for making the diagnosis of AS. Inflammatory changes in the appendicular joints and entheses are less frequent and less severe (Fig. 5) (*3,6*).

Psoriatic arthritis is a polyarticular asymmetric disorder affecting the synovial joints of the appendicular skeleton with predilection for the interphalangeal joints of the foot and hand associated with enthesopathy of the axial and appendicular skeleton (Fig. 6). Psoriasis must have been diagnosed in those patients. The spondylitis of PA and reactive arthritis are characterized by asymmetric paravertebral ossifications mostly at the lower thoracic and upper lumbar spine affecting mainly the lateral aspect of the vertebral bodies (*7*).

Reactive arthritis is also a polyarticular asymmetric inflammatory disorder, but it affects mainly the large joints and entheses in the lower extremity (Fig. 7). Involvement of the upper extremity joints is unusual (Fig. 4). It is characterized by arthritis presenting within 4 wk after nongonococcal urethritis or cervicitis or by arthritis presented within 6 wk after acute diarrhea. In the presence of increased antibody titer of a triggering organism, usually chlamydia, yersinia, salmonella or campylobacter (*4,5*), the term Reiter's disease is more appropriate. The classic triad of arthritis, urethritis and conjunctivitis are present in a minority of patients.

Bone scintigraphy can provide objective evidence of an inflammatory process at the entheses. There is a paucity of publications concerning scintigraphic findings and their value in enthesopathies (*8–12*). Tendons and ligaments are attached to the bone by the Sharpey's fibers that are collagen fibers of the mineralized fibrocartilage structure of a tendon or ligament that will eventually mix with those of the bone matrix (*1,2*).

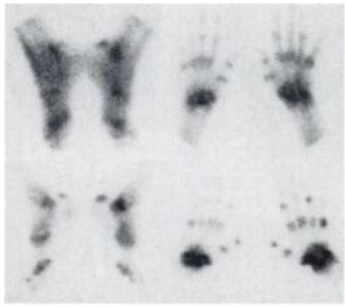

FIGURE 6. A 37-yr-old woman with psoriatic arthritis. Blood-pool images in the medial view of the foot show increased blood pool in several metatarsal phalangeal joints and at the calcaneus in both feet (top left). Blood-pool images of the hands show increased blood pool in several metacarpal phalangeal, interphalangeal and wrist joints of both hands (top right). Delayed images of the foot in the medial view show increased uptake in several metatarsal phalangeal joints and ankle joints due to synovial inflammation and increased uptake at the insertion site of the achilles tendon in both calcaneus due to enthesopathy (bottom left). Delayed images of the hands show increased uptake due to synovial inflammation in several metacarpal phalangeal, interphalangeal and wrist joints of both hands (bottom right).

FIGURE 7. Delayed images of the knees in the anterior (top), right medial (bottom left) and left medial (bottom right) of Patient 2 show increased uptake in the left knee due to synovial inflammation.

Entheses are metabolically active and can act like the periosteum of bone at their insertion sites. A disease process at these sites may involve a periosteal reaction causing increased osteoblastic activity (*2*). Pathologically, the inflammatory process at an enthesis consists of inflammatory granulation tissue that is gradually replaced by fibrocartilage and later by ossification (*4*). This will result in increased focal ^{99m}Tc-MDP uptake at the bony attachment site shown by scintigraphy. Bone remodeling may persist a long time after the inflammation subsided. The acquisition of dynamic examinations of blood flow and blood pool is necessary to assess the chronicity of the lesion (*13,14*). Since the decision to perform a three-phase bone scintigraphy must be made, we have been performing early scans routinely in patients referred for evaluation of a painful joint or bone. The hyperemia and local abnormalities of permeability associated with the inflammatory process cause increased blood flow and blood pool in the early phases of the bone scan (vascular phase and extracellular fluid phase). The absence of abnormal uptake in the early scans indicates a more inactive process (*13*).

The value of bone scintigraphy relies on its ability to identify symptomatic or asymptomatic areas of abnormal tracer uptake representing areas of active disease and to recognize the extent of systemic inflammatory disease. Focally increased activity in the delayed images restricted to sites of tendon or ligament insertions associated with increased blood flow and blood pool in the early images is typical of enthesopathy (*15*). The association of enthesopathy with joint involvement on bone scan, as in the cases presented here, readily suggests the diagnosis of inflammatory spondyloarthropathy. The scintigraphic appearance in the appropriate clinical setting seems to be very characteristic in the diagnosis of enthesopathy related to inflammatory spondyloarthropathy.

CONCLUSION

Bone scintigraphy contributes to the initial evaluation of these patients by indicating the extent and activity of the disease. Early involvement of several joints and entheses can be shown by bone scintigraphy before any clinical sign or radiological feature of bone erosion and proliferation develop. The patterns of enthesopathy should be recognized on a bone scan.

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