Leukocyte Scanning With ^{111}In Is Superior to Magnetic Resonance Imaging in Diagnosis of Clinically Unsuspected Osteomyelitis in Diabetic Foot Ulcers

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OBJECTIVE— To compare the accuracies of MRI and leukocyte scanning in diagnosing clinically unsuspected osteomyelitis in diabetic foot ulcers.

RESEARCH DESIGN AND METHODS— A prospective study of 16 diabetic foot ulcers in 12 patients, including both ambulatory and hospitalized patients, was performed at a university medical center. Pedal images were obtained by leukocyte scanning with [^{111}In]oxyquinoline and MRI. Definitive diagnosis of osteomyelitis then was determined by bone biopsy for culture and histology.

RESULTS— Biopsy-proven osteomyelitis was present in 7 (44%) of the 16 foot ulcers. The diagnosis was suspected clinically in 0%. Leukocyte scanning was 100% sensitive, whereas MRI was only 29% sensitive in diagnosing osteomyelitis in diabetic foot ulcers. Specificities were 67 and 78%, respectively. The positive and negative predictive values (70 and 100%, respectively) for the leukocyte scan also were greater than those of MRI (50 and 58%, respectively).

CONCLUSIONS— Leukocyte scanning is superior to MRI in detecting clinically unsuspected osteomyelitis in diabetic foot ulcers.

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MRI, MAGNETIC RESONANCE IMAGING; T1WI, T1 WEIGHTED IMAGES; SE, SPIN ECHO; T2WI, T2 WEIGHTED IMAGES; TR, REPETITION TIME; TE, ECHO TIME; WBC, WHITE BLOOD CELL.

Early diagnosis of osteomyelitis in diabetic foot ulcers is important as prompt antibiotic treatment has been shown to decrease the rate of amputation (1). However, determining this diagnosis is often difficult. We have shown previously that clinical diagnosis frequently is inadequate and fails to detect 68% of those with osteomyelitis (2). Of the noninvasive imaging tests, leukocyte scans with [^{111}In]oxyquinoline have been shown to be more sensitive than bone scans or radiographs in diagnosing unsuspected osteomyelitis in diabetic foot ulcers (2,3). Although MRI has been shown to be sensitive and specific in diagnosing osteomyelitis in severely infected diabetic foot ulcers (4,5), it has not been evaluated in clinically unsuspected osteomyelitis, nor has it been compared with leukocyte scans. We, therefore, compared the sensitivities and specificities of leukocyte scans and MRI for diagnosing clinically unsuspected osteomyelitis in diabetic foot ulcers and found the leukocyte scan to be superior.

RESEARCH DESIGN AND METHODS

— Twenty-three patients with diabetes and foot ulcers were evaluated at Mount Sinai Medical Center from September 1989 to June 1990; 12 patients with 16 foot ulcers were included in the study. Of the foot ulcers, 94% (15/16) were in outpatients. The ^{111}In leukocyte scan results on 11 ulcers were included in a prior publication (2). Exclusion criteria determined on the basis of possible risks of bone biopsy included myocardial infarction in the previous 6 mo (n = 1), severe peripheral vascular disease (ankle-brachial index <50%; n = 3), ongoing antibiotic treatment for >7 previous days (n = 4), or patient declining to participate (n = 3). The protocol was approved by the Mount Sinai School of Medicine Institutional Review Board and written consent was obtained from participants.

The referring physician was asked to render a clinical opinion about

Table 1—*Clinical and physical characteristics of 16 diabetic foot ulcers in 12 patients*

Ulcer characteristic	Assessment measure [median (range) or % (ratio)]
Duration (wk)	52 (range, 1–364)
Inflammation (%)	12.5 (2/16)
Size (cm^2)	0.5 (range, 0.25–0.35)
Depth (%)	
Shallow*	75 (12/16)
Moderately deep†	19 (3/16)
Exposing bone‡	6 (1/16)
Underlying osteomyelitis (%)	
Diagnosis by bone biopsy	44 (7/16)
Clinical diagnosis	0 (0/16)

*Shallow—ulcer <3 mm deep.
†Moderately deep—ulcer not exposing bone but >3 mm deep.
‡Exposing bone—ulcer exposing bone visually or with probing.

whether osteomyelitis was present in each case. Before bone biopsy and culture, all patients underwent leukocyte imaging and MRIs. All patients then underwent bone biopsy for pathology and culture. The bone radiologist, pathologist, and nuclear medicine physician read their respective tests blinded to the other test results.

Imaging techniques

Leukocyte images were acquired in the dorsal and plantar positions 24 h after the injection of 500 μCi of mixed autologous leukocytes, labeled with [^{111}In] oxyquinoline. Studies were classified as positive for osteomyelitis when focally increased activity was present on both the dorsal and plantar images at 24 h.

MRIs of the involved foot were performed using a 0.5 superconducting magnet (Gyrex 5000 Elscint, Haifa, Israel). Surface coils were used in all cases. Images were obtained on the axial and coronal or sagittal planes. Data were collected on a 256-by-256 matrix interpolated to 512-by-512 for display. Section thickness varied between 7 and 12 mm. T1WIs included SE 400–600 ms TR and 16–30 ms TE; and T2WI included SE 1800–2000, 30 ms TR, and 80 ms TE. Studies were considered positive for osteomyelitis if signal intensity decreased on T1WI and increased on T2WI in the bone in the area of the foot ulcer.

Bone biopsies

Bone specimens for pathology and culture were obtained in all 16 ulcers. Bone biopsies were performed with a 15-gauge trocar placed through a 5-mm incision in an area of skin noncontiguous with the foot ulcer. Sterile technique and local anesthesia were used.

Diagnosis of osteomyelitis

The diagnosis of osteomyelitis was based on a positive bone culture and/or pathological criteria for osteomyelitis. Pathological diagnosis required the presence of all three criteria, including: osteonecrosis (the absence of osteocytes in their lacunae in the presence of nuclear staining for other cells in the section), marrow fibrosis, and inflammatory cells.

Statistics

We used χ^2 or Fischer's exact tests, and the McNemars test (based on the sign test, one-tailed) where appropriate. Significance was defined as $P < 0.05$.

RESULTS

Diagnosis of osteomyelitis

Osteomyelitis was present in the bone in 44% (7/16) of the diabetic foot ulcers in this study. The diagnosis of osteomyelitis was made by positive culture alone in 5 cases, and both positive culture and pathology in 2 cases. Osteomyelitis was diagnosed clinically in 0% (0/7).

Physical examination and laboratory evaluation

Table 1 reveals the benign clinical appearance of the majority of the ulcers—most were small, shallow, and noninflammed. The results of the laboratory tests presented in Table 2 also illustrate the clinically benign presentation of the patients with diabetic foot ulcers in this study.

Imaging tests

The leukocyte scan was 100% sensitive for diagnosing osteomyelitis in these diabetic foot ulcers, in contrast to a sensi-

Table 2—*Results of laboratory tests for the 16 ulcers*

Laboratory value	Mean ± SE	Normal range
Alkaline phosphatase (U/L)	102 ± 29	30–110
ESR (mm/h)	45 ± 36	0–30
WBCs	7.6 ± 2.1 × 10^3	4.8–10.8 × 10^3
HbA_{1c} (%)	10.4 ± 3.4	5–7
Glucose (mM)	11.03 ± 5.49	3.36–6.72

Table 3—*Results of WBC scan versus MRI in diagnosis of osteomyelitis in diabetic foot ulcers*

				Predictive value	
	Sensitivity	Specificity	Accuracy	Positive	Negative
WBC scan (%)	100 (7/7)	67 (6/9)	81 (13/16)	70 (7/10)	100 (6/6)
MRI (%)	29 (2/7)*	78 (7/9)	56 (9/16)	50 (2/4)	58 (7/12)

*P = 0.03.

tivity of only 29% for MRI (Table 3) ($P = 0.03$). The MRI correctly detected an underlying osteomyelitis in only 2 ulcers. One of these ulcers was exudative, and we were able to probe to bone. The other ulcer was moderately deep and not inflamed. The specificities of the tests were similar: 67% for leukocyte scan, 78% for MRI. Table 3 demonstrates the superior positive and negative predictive values of leukocyte scans versus MRI. No significant relation was noted between a positive MRI or leukocyte scan and ulcer inflammation, ulcer size, or bone histology.

CONCLUSIONS— Timely diagnosis and treatment of osteomyelitis in diabetic foot ulcers are crucial as early antibiotic treatment can be curative and prevent amputation (1). Bone biopsy for culture and pathology is the gold standard for diagnosis of osteomyelitis, but this invasive technique may present a risk in the diabetic foot (6). An accurate noninvasive diagnostic test would eliminate this risk. In a prior prospective study (2), we found that clinical diagnosis is inadequate, as only 32% (9/28) of the cases of underlying osteomyelitis in diabetic foot ulcers were detected clinically. However, leukocyte scans were found to be accurate in diagnosing osteomyelitis in diabetic foot ulcers, and were superior to both radiographs and bone scans. Results from this study expand these findings by demonstrating that leukocyte scanning is also superior to MRI in clinically unsuspected osteomyelitis in diabetic foot ulcers.

Three retrospective (4,7,8) and one prospective (5) study revealed a high sensitivity and specificity (although the latter was decreased in Charcot joints) of MRI for diagnosing severe, progressive osteomyelitis in diabetic foot ulcers. In contrast, our results reveal that MRI has a low sensitivity in diagnosing clinically unsuspected osteomyelitis in diabetic foot ulcers. Leukocyte imaging had greater sensitivity and predictive values than MRI. One of the 2 cases of osteomyelitis detected by MRI was underlying the only ulcer in which bone could be probed, adding further evidence that the sensitivity of MRI is related directly to the severity of osteomyelitis in diabetic foot ulcers. These 2 cases also were detected by leukocyte scanning.

Three leukocyte scans were false-positive, all in noninflamed ulcers. In 2 of the 3 patients, the referring physician chose, on the basis of the positive leukocyte scan, to treat for osteomyelitis with 4–6 wk of ciprofloxacin and metronidazole, despite the negative biopsy. These ulcers healed within the treatment period. The third patient was not treated with antibiotics, and his ulcer has remained stable and unhealed for 18 mo. Hence, it is possible that the leukocyte scans in these patients were really true positives, but either the small specimen size of bone biopsy missed the area of osteomyelitis, or the organism, such as an anaerobe, was difficult to grow in culture.

In conclusion, leukocyte scanning is superior to MRI in diagnosing clinically unsuspected osteomyelitis in diabetic foot ulcers. A previous study (2) has shown that 100% of diabetic foot ulcers that expose bone have an underlying osteomyelitis. Therefore, these patients should be treated for osteomyelitis and do not require leukocyte scanning for diagnosis. Because the majority of ulcers that do not expose bone also will have an underlying osteomyelitis (2), these patients should undergo leukocyte scanning for early and definitive diagnosis of this treatable and common precursor of amputation.

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