Appearance of Acute Gouty Arthritis on Indium-111-Labeled Leukocyte Scintigraphy

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Indium-111-labeled leukocyte scintigraphy was performed on a 66-yr-old male with polyarticular acute gouty arthritis. Images revealed intense labeled leukocyte accumulation in a pattern indistinguishable from septic arthritis, in both knees and ankles, and the metatarsophalangeal joint of both great toes, all of which were involved in the acute gouty attack. Joint aspirate as well as blood cultures were reported as no growth; the patient was treated with intravenous colchicine and ACTH for 10 days with dramatic improvement noted. Labeled leukocyte imaging, repeated 12 days after the initial study, revealed near total resolution of joint abnormalities, concordant with the patient's clinical improvement. This case demonstrates that while acute gouty arthritis is a potential pitfall in labeled leukocyte imaging, in the presence of known gout, it may provide a simple, objective, noninvasive method of evaluating patient response to therapy.

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Indium-111- (^{111}In) labeled leukocyte scintigraphy is a useful radionuclide procedure for the diagnostic evaluation of musculoskeletal sepsis. In order to maximize the utility of this procedure, individuals interpreting labeled leukocyte imaging must be aware of potential pitfalls that affect the sensitivity or specificity of the procedure. The following report presents the results of labeled leukocyte imaging in a case of acute gouty arthritis: as a potential pitfall, as well as a method of monitoring patient response to therapy.

CASE REPORT

A 66-yr-old male was admitted to our institution with a chief complaint of severe, polyarticular pain of six days duration. Physical examination of the patient revealed marked erythema, swelling and tenderness of both knees and ankles, as well as the metatarsophalangeal joint of both great toes. Radiographs of the knees were normal. Laboratory values were remarkable for a leukocytosis of 16,000 per mm^3 (81 polymorphonuclear leukocytes, 16 lymphocytes, 3 basophils), an erythrocyte sedimentation rate of 86 mm/hr (normal <12 mm/hr), and serum uric acid of 13.4 mg/dl (normal: 4–8 mg/dl). Aspiration of the right knee yielded 30 cc of serosanguineous fluid with 52,000 leukocytes per mm^3 (93 polymorphonuclear leukocytes, 5 monocytes, 1 lymphocyte, 1 eosinophil) as well as sheets of urate crystals. Gram stain of the aspirate was negative. Cultures of the aspirate were reported as no growth. The diagnosis of polyarticular acute gouty arthritis was made, and intravenous (i.v.) colchicine therapy was begun. On the second day after admission, the patient became febrile to 39°C, and his leukocyte count rose to 23,000 per mm^3. An ^{111}In-labeled leukocyte study was requested to exclude superimposed infection.

Twenty-four hours postinjection of 18.5 MBq (500 μCi) of autologous white cells labeled with ^{111}In-oxine according to the method of Thakur et al. (*1*), whole-body imaging was performed on a large field of view gamma camera, equipped with a medium-energy collimator. Energy discrimination was accomplished by 20% windows centered over the 174- and 247-keV photopeaks of ^{111}In. Intense accumulation of labeled white cells was seen in both knees, ankles, and both first metatarsophalangeal joints, corresponding to the joints affected by acute gouty arthritis (Fig. 1).

Blood and urine cultures performed at the same time were subsequently reported as no growth, and the patient was treated with i.v. ACTH and colchicine. Over the next 10 days he defervesced, his leukocyte count returned to normal, and there was marked clinical improvement as the acute attack subsided; minimal bilateral knee pain did persist however. Indium-111-leukocyte imaging repeated 12 days after the initial study revealed faint uptake in both knees, concordant with the clinical impression of resolving acute gouty arthritis (Fig. 2).

DISCUSSION

Gouty arthritis is a complication of prolonged hyperuricemia; acutely it is characterized by recurrent episodes of severe joint inflammation which, if untreated, progress to tophaceous gout with joint deformities and disabilities, renal calculus formation and eventually, renal failure (*2*). The initial presentation of acute gouty arthritis is usually monoarticular, and typically involves the lower extremities, especially the first metatarsophalangeal joints, the ankles, and the knees. Involvement of the hips, spine and upper extremities is uncommon (*3*).

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FIGURE 1
Anterior 24-hr whole-body ^{111}In-labeled leukocyte image demonstrates marked uptake of labeled leukocytes in both knees, ankles, and first metatarsophalangeal joints, corresponding to those joints involved by acute gouty arthritis. Nasal uptake was due to rhinitis. Penile (urethral) uptake was attributed to inflammation secondary to a urinary drainage catheter. Urine cultures were reported as no growth.

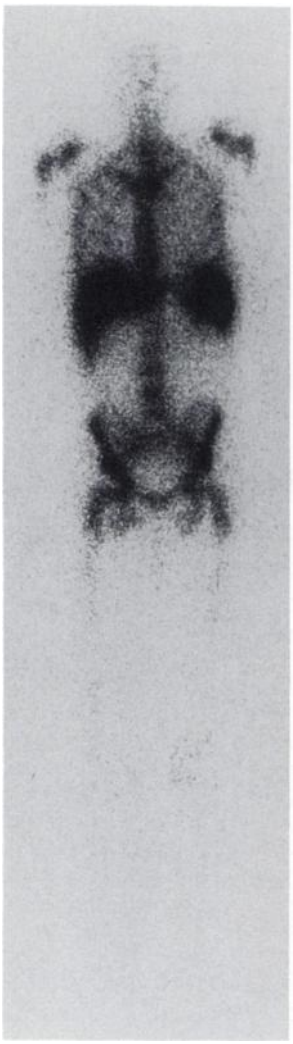

FIGURE 2
Anterior 24-hr whole-body image performed 12 days after Figure 1 reveals minimal activity in the left knee joint and right suprapatellar bursal region. Findings were interpreted as consistent with minimal residual inflammation, and were concordant with the clinical impression of improvement.

Pathologically, acute gouty arthritis is the result of an intense inflammatory response induced by microcrystals of monosodium urate monohydrate in the joint cavity. In essence in acute gouty arthritis leukocytes, whose role is that of body defense, are actually the perpetrators of damage to the body and the mechanisms that stimulate leukocyte function augment the damage they cause. Successful therapy with both colchicine and ACTH is based upon the ability of these drugs to inhibit the chemotactic response of leukocytes, thereby arresting the inflammatory process (*2,4*).

Clinically, the onset of joint inflammation in acute gout is sudden and peaks within 24 hr. Affected joints are exquisitely tender and painful; considerable swelling and erythema about the joints are also generally present. When accompanied by fever and leukocytosis, it may not be possible to distinguish acute gouty arthritis from septic arthritis or cellulitis, and aspiration of the involved joint is then indicated.

Indium-111-labeled leukocyte imaging is a useful tool in the diagnosis of musculoskeletal sepsis (*5,6*). Despite its utility, false-positive results have been reported in normal variants, tumors, fractures, and during radiation therapy (*7–10*). Uptake in secondary gout has also been observed (*11*). It is essential that the individual interpreting labeled leukocyte images be cognizant of these potential pitfalls if the diagnostic utility of the procedure is to be maximized. The case presented demonstrates that acute gouty arthritis has another potential pitfall: the strikingly abnormal labeled leukocyte image produced by this malady is one that, especially when monoarticular, may be indistinguishable from septic arthritis; consequently the diagnosis of septic arthritis should be made by cultures of the joint aspirate in the presence of a history of gout.

A similar lack of specificity has been reported for other radionuclide procedures in the presence of gout. Abnormal but nonspecific findings and uptake patterns, indistinguishable from Paget's disease, metastasis, and septic arthritis, have been observed on bone and gallium scintigraphy performed on patients with gout (*12–14*);

the role of these procedures in gouty arthritis is therefore limited.

Unless joint aspiration is performed, response to treatment is judged subjectively, i.e., symptomatic improvement. In an effort to objectively, and noninvasively, evaluate the patient's response to therapy, a second labeled white cell study was performed after treatment. This follow-up study demonstrated a dramatic decrease in the polyarticular accumulation of labeled leukocytes, correlating well with the patient's subjective improvement. This follow-up study suggests that in the presence of known acute gouty arthritis, ^{111}In-labeled leukocyte imaging may offer a simple, noninvasive, objective, method of evaluating and documenting a patients' response to therapy.

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Editorial: Radionuclide Imaging of Joint Inflammation in the '90s

Although technetium-99m- (^{99m}Tc) MDP bone scans have been used for years to diagnose septic and aseptic arthritis, Palestro et al. in this issue suggests using leukocyte scans to follow the therapeutic response of patients with gouty arthritis (*1*). This raises the question of what new radionuclide modalities will be applied to imaging joint inflammation in the 1990s and how they will relate to standard ^{99m}Tc-MDP bone scans.

One of the newest and most exciting modalities is radiolabeled immunoglobulin (IgG). Radiolabeled antibodies directed against tumor antigens have been used to diagnose metastases since Pressman's original report in 1957 (*2*), but it was not until 1988 that Rubin and colleagues applied antibodies to infection imaging (*3*). Fortunately, some of the difficulties of developing immunoglobulins for tumor imaging are not as formidable for infection imaging. First, developing antibodies to microbial antigens that will not cross-react with normal human cells appears easier than the search for tumor-specific antigens. This allows a high target-to-background ratio making lesions easier to detect. Second, while microvascularity to tumors is quite variable, acute inflammation is associated with increased blood flow and permeability, enhancing delivery of radiolabeled immunoglobulins. Microbial antigens don't modulate as frequently as tumor cells increasing chances to pick up metastatic sites of infection. And, finally, antibodies can be directed against leukocytes that accumulate at the site of infection rather than against each specific type of organism (*3*).

Originally, an iodine-125-labeled murine monoclonal antibody of the IgG_1 sub-class specific for an epitope on Fisher Type 1 *pseudomonas aeruginosa* was used in rat thigh infections (*3*). Uptake was seen as early as 4 hr and increased through 196 hr. To compare with nonspecific antibody uptake, a second nonspecific murine antibody directed against the *p*-arsanilic acid haptene was used as a control. Amazingly, the nonspecific antibody had degrees of uptake identical to the

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