INVESTIGATIVE NUCLEAR MEDICINE

Donor-Leukocyte Imaging in Granulocytopenic Patients with Suspected Abscesses: Concise Communication

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Indium-111-labeled donor leukocytes were used for the detection of foci of suppuration in eight severely leukopenic patients with marrow suppression, either idiopathic or associated with chemotherapeutic regimens for leukemia. In three patients good correlation was found between the results of imaging and clinical signs or subsequent proof of inflammation. In the other five patients, in whom no evidence of localized suppuration occurred, no abnormal accumulations of radioactivity were demonstrable. Labeled donor leukocytes provide a method for locating suppurative foci in severely leukopenic patients in whom autologous leukocyte labeling is impractical.

J Nucl Med 23: 319–321, 1982

Abscesses frequently occur in patients with bone-marrow depression, and the location is often difficult to identify since these patients may present with fever and sepsis without signs indicating the site of abscess formation. For determination of appropriate therapy and to determine whether surgery is needed, a technique for detection of sites of infection is needed. Since viable, actively phagocytic leukocytes are attracted to most bacterial infections, a technique for labeling granulocytes with radionuclides and the imaging of the granulocyte distribution should reveal sites of infection if significant accumulation of labeled leukocytes occurs. Recently, autologous leukocytes labeled with indium-111 oxine have been found to locate abscesses accurately (*1*,*2*). Since there are so few granulocytes in leukopenic patients with suspected abscesses, we have obtained granulocytes from donors by a standard leukapheresis procedure, labeled them with indium-111, and imaged their distribution in the patients.

This paper presents data from eight patients under chemotherapy for malignant disease, all of whom demonstrated objective, but not necessarily localized, signs of active infection and were at the same time severely leukopenic (<300 granulocytes/mm^3). Attempts were made in these patients to locate the site of infection by scanning with In-111-tagged donor leukocytes.

METHODS

In each study, leukocyte concentrates were prepared by interrupted-flow leukapheresis* with hydroxyethyl starch as a red-cell sedimenting agent, a technique previously described by Heustis (*3*). Leukocyte packs produced by this method contained 1.5–2.6 × 10^{10} leukocytes in a volume of approximately 400 ml.

Indium-111 oxine was prepared by adding indium-111 chloride (approximately 1 mCi) to an equal volume of distilled water and 200 μl of 0.3 *M* acetate buffer at pH 5.0. Fifty micrograms of oxine solution (1 mg/ml in absolute ethanol) were added and thoroughly mixed in. The activity was extracted into an equal volume of chloroform, and the solvent evaporated to dryness. The chelated activity was redissolved in 100 μl of absolute ethanol and diluted to a final volume of 500 μl with normal saline.

From the leukocyte pack otained from the leukapheresis procedure, 20 ml were withdrawn into a syringe, which was then placed upright, needle uppermost, for

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Received Sep. 28, 1981; revision accepted Nov. 20, 1981.

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45 min to allow any contaminating red blood cells to settle out. No additional sedimenting agent was added. The leukocyte-rich supernatant plasma was then expressed through sterile plastic tubing into sterile centrifuge tubes. The leukocyte-rich plasma was spun at 450 *g* for 5 min, the supernatant discarded, and the leukocytes gently resuspended in 3 ml of 50% plasma in saline.

The 500 μl of indium-111 oxine solution was added to the leukocyte suspension and incubated at room temperature (22 °C) for 25 min with occasional agitation. The labeled cells were then centrifuged at 450 *g* for 5 min. The supernatant was removed and the activities of the cell button and supernatant were determined separately. Two milliliters plasma were layered over the cell button and very carefully withdrawn. The cells were finally resuspended in approximately 4 ml of plasma, and an aliquot of this final suspension was removed for a cell count and a microscopic assessment of any white-cell clumping. The dose was then calibrated so that between 200 and 500 μCi of activity were administered intravenously. Images were obtained 16–24 hr after the dose using a large-crystal camera.

RESULTS

In this study eight patients under chemotherapy for malignant disease were studied, all of whom had (a) overt symptoms and signs suggestive of an active infection, (b) severely depressed bone-marrow function, and (c) severe leukopenia, with granulocyte counts of less than 300/mm^3.

The labeling efficiency (leukocyte-bound activity over total activity) varied between 55 and 85%, with the highest percentage occurring in the preparation with the largest number of leukocytes. Our labeling efficiency is lower than reported in some other studies since we are labeling in plasma, which decreases labeling efficiency (*1*,*4*,*5*). The number of leukocytes administered in the labeled preparation ranged from 5.2×10^8 to 1.1×10^9. There was no microscopic evidence of leukocyte clumping in any of the preparations.

Of the eight patients studied, five had normal scans, and no evidence of localized inflammation was obtained by physical examination, chest x-ray, or clinical course. Three of the five patients with normal leukocyte scans had normal abdominal computed tomographic scans, and the other two had normal abdominal ultrasound examinations. Three patients had evidence of localized infection and all had abnormal scans. One of these patients had a supraclavicular abscess in a region of previous lymph-node biopsy. The histories of the other two abnormal patients are included in the following presentations.

Case 1. A 35-yr-old man with a diagnosis of acute myelocytic leukemia was readmitted in apparent blast crisis: white-cell count 69,000, with 68% blasts, 22% lymphocytes, 3% monocytes, and 7% granulocytes. The patient was started on chemotherapy for treatment of the blast crisis. During this repeat course of chemotherapy, he developed chills and a high, spiking fever of 39.5 °C. At the time of development of these signs, the absolute granulocyte count was less than 300/mm^3. An indium-111 donor leukocyte study was performed and images at 24 hr after administration of labeled leukocytes revealed significant accumulations in the perirectal (Fig. 1) and left mandibular regions. A perirectal abscess

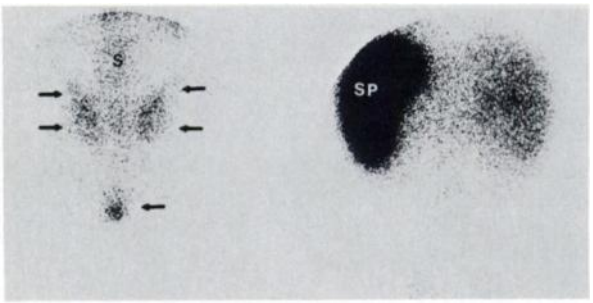

FIG. 1. Posterior indium-111 leukocyte images of the pelvis (left) and abdomen (right) demonstrating an abnormal focal accumulation (arrow) in a perirectal abscess. Normal accumulations in sacroiliac joints (double arrows), spine (S), liver (L), and spleen (SP) are noted.

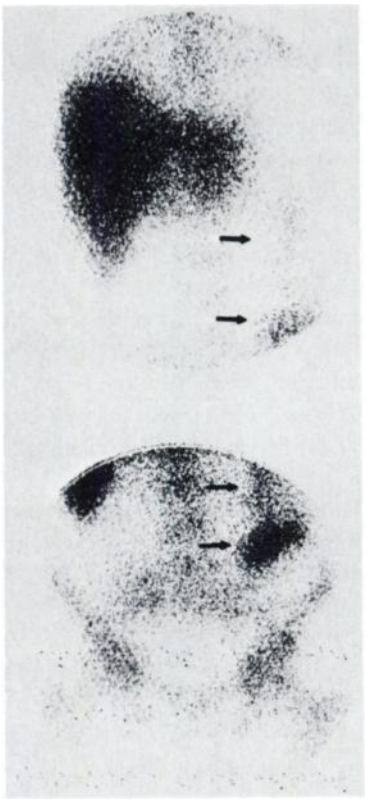

FIG. 2. Anterior indium-111 leukocyte images of the abdomen (upper) and pelvis (lower). Abnormal accumulation is seen in left upper pelvic and midabdominal areas (arrows). Normal accumulation is noted in liver on abdominal image, and in bone marrow of spine, pelvis, and proximal femurs in lower image.

was then clinically identified and surgically drained. Cultures of the abscess grew *E. coli*. The mandibular accumulation was related to a gingivitis, which resolved on antibiotic therapy.

Case 2. A 34-yr-old man with a 2½-yr history of chronic myelocytic leukemia was admitted in blast crisis. During his hospital course, he underwent splenectomy for massive splenomegaly and severe, persistent thrombocytopenia complicated by persistent epistaxis. Following surgery, he was started on a chemotherapy protocol for his blast crisis. On the eighteenth postoperative day he became febrile, and blood cultures grew *E. coli*, an enterobacter organism, and an enterococcus. Treatment with carbenicillin and tobramycin produced rapid defervescense. A few days later, however, the patient again became febrile with an intermittent fever reaching 40 °C. All blood cultures were negative and localizing signs were totally absent at this time. An indium-111 donor leukocyte study was conducted, revealing an abnormal accumulation in the left midabdominal region (Fig. 2). The patient, being persistently pancytopenic, was continued on antibiotics and daily granulocyte transfusions. In a few days he developed left abdominal pain. A computed tomographic study confirmed the presence of an abscess, which was surgically drained. After further combined antibiotic therapy and granulocyte transfusions, he became afebrile and antibiotics were discontinued.

DISCUSSION

The use of indium-111 oxine for labeling autologous leukocytes has been described previously (*1*,*2*,*4*,*6*,*7*). Experimental studies locating induced abscesses in animals demonstrated the feasibility of the technique and suggested its clinical application (*4*,*6*), and several subsequent studies showed the value of using labeled autologous leukocytes in identifying abscesses in patients (*1*,*2*,*7*). A study of 64 patients by McDougall et al. (*2*) included four leukopenic patients who were studied with indium-111-labeled donor leukocytes. In two of these patients, focal accumulations of radioactivity were observed, and in one of them the presence of an abscess was subsequently proven.

Dutcher et al. (*8*) have recently studied 14 granulocytopenic patients with known sites of infection. They used homologous, ABO-matched granulocytes labeled with indium-111. Thirteen of the 14 patients had abnormal accumulation at the site of infection at 30 min, and all 14 patients had abnormal studies 24 hr after administration. We did not image our patients until 16–24 hr after administration, so we are unable to say whether the abnormalities could be detected earlier. Furthermore, our patients did not have known sites of infection before the study. Previously, we found that some abscesses could not be detected on images obtained 2–4 hr after administration of indium-111 autologous leukocytes but were detected on images obtained at 16–24 hr (*5*).

In eight cases studied in this series, donor leukocytes labeled with indium-111 oxine were used exclusively. The distribution of the donor leukocytes was similar to the distribution observed in studies using autologous leukocytes. In five of these patients, no localizing accumulations were found and no localized inflammatory foci were discovered clinically. In the other three cases definite focal accumulations of radioactivity occurred and conformed to local areas of phlegmonous inflammation or abscess formation.

This preliminary study demonstrates that, in severely leukopenic patients, indium-111-labeled donor leukocytes can be used successfully as a tracer for the detection of areas of inflammation, including abscesses. In patients undergoing granulocyte transfusions, it is quite simple for the laboratory doing indium-111 oxine labeling to label the donor leukocytes. The cells maintained viability and chemotactic function, since they were able to accumulate in inflammatory processes. It is felt that this technique is a useful adjunct for abscess delineation in severe leukopenia, when autologous leukocyte labeling is impractical.

FOOTNOTE

* Haemonetics Model 30 Machine.

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