Vertebral SPECT's superiority in detecting extra-vertebral body metastasis may be because the pedicle, lamina and processes consist mainly of compact bone, which is favorable for vertebral SPECT, but not for MRI. Compact or cortical bone metastases may be more common than previously expected (*17*). There is, however, a drawback to vertebral SPECT: lower specificity. In non-neoplastic bone diseases, ^{99m}Tc-labeled phosphate agents often accumulate in congruence with the facet joint, vertebral endplate and osteophyte. Holder et al. (*18*) reported that high-resolution SPECT bone imaging is useful in diagnosing facet syndrome. As shown by Even-Sapir et al. (*19*), sites and patterns of accumulation in vertebral SPECT may be helpful in differentiating metastasis from degenerative joint disease or other benign bone diseases.

When spinal MRI has already been performed, whole-body bone scintigraphy should be performed, because osseous metastases remote from the thoracolumbar spine are frequent. Performing skeletal scintigraphy would also be helpful in confirming suspected false-positive MRI. We believe that patients with equivocal or negative planar bone imaging in spite of back pain should immediately undergo vertebral SPECT because of its greater ability to detect metastasis, especially extra-vertebral body metastasis.

CONCLUSION

Vertebral SPECT, using a high-resolution SPECT camera, produces excellent results, comparable to and complementary with MRI in detecting vertebral metastases. Vertebral SPECT might be superior to MRI in detecting extra-vertebral body metastases. Bone scan is the method of choice to screen for osseous metastases, but high-resolution vertebral SPECT should be performed without hesitation when there is equivocal uptake in the vertebra on planar imaging or a patient has symptoms despite normal scintigraphic and/or MRI findings. We should not, however, neglect MRI, mainly because it offers significant additional information on the dura and spinal cord.

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REFERENCES

1. Avrahami E, Tadmor R, Dally O, Hadar H. Early MR demonstration of spinal metastases in patients with normal radiographs and CT and radionuclide bone scans. *J Comput Assist Tomogr* 1989;13:598–602.
2. Delbeke D, Powers TA, Sandler MP. Negative scintigraphy with positive magnetic resonance imaging in bone metastases. *Skeletal Radiol* 1990;19:113–116.
3. Bretill J. Skeletal scintigraphy for the diagnosis of malignant disease to the bone. In: Goris ML, ed. Sensitivity and specificity of common scintigraphic procedures. London: Year Book Medical Publishers; 1985:49–67.
4. Frank JA, Ling A, Patronas NJ, et al. Detection of malignant bone tumors: MR imaging versus scintigraphy. *AJR* 1990;155:1043–1048.
5. Alga PR, Bloem JL, Tissing H, Falke TH, Arndt JW, Verboom LJ. Detection of vertebral metastases: comparison between MR imaging and bone scintigraphy. *Radiographics* 1991;11:219–232.
6. Mehta RC, Wilson MA, Perlman SB. False-negative bone scan in extensive metastatic disease. CT and MR findings. *J Comput Assist Tomogr* 1989;13:717–719.
7. Kattapuram SV, Khurana JS, Scott JA, El-Khoury G. Negative scintigraphy with positive magnetic resonance imaging in bone metastasis. *Skeletal Radiol* 1990;19:113–116.
8. Gosfield E III, Alavi A, Kneeland B. Comparison of radionuclide bone scans and magnetic resonance imaging in detecting spinal metastases. *J Nucl Med* 1993;34:2191–2198.
9. Brown B, Laorr A, Greenspan A, Stadalnik R. Negative bone scintigraphy with diffuse osteoblastic breast carcinoma metastases. *Clin Nucl Med* 1994;19:194–196.
10. Murray PC. The role of SPECT in the evaluation of skeletal trauma. *Ann Nucl Med* 1993;7:1–9.
11. Ryan PJ, Fogelman I, Gibson T. Scintigraphy with SPECT in chronic low back pain. *J Nucl Med* 1991;32:913.
12. Kanmaz B, Liu Y, Uzum F, et al. SPECT versus planar bone scintigraphy in patients with low back pain. *J Nucl Med* 1992;33:868.
13. Gates GF. SPECT imaging of the lumbosacral spine and pelvis. *Clin Nucl Med* 1988;13:907–914.
14. Galasko CSB. Skeletal metastases and mammary cancer. *Ann R Coll Surg Engl* 1972;50:3–28.
15. Silberstein EB, Saenger EL, Tofe AJ. Imaging of bone metastasis with ^{99m}Tc-Sn-EHDP(diphosphonate), ^{18}F and skeletal radiography. *Radiology* 1973;107:551–555.
16. Modic MT, Steinberg PM, Ross JS, Masaryk TJ, Carter JR. Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. *Radiology* 1988;166:193–199.
17. Hendrix RW, Rogers LF, Davis TM. Cortical bone metastases. *Radiology* 1991;181: 409–413.
18. Holder LE, Machin JL, Asdourian PL, Links JM, Sexton CC. Planar and high-resolution SPECT bone imaging in the diagnosis of facet syndrome. *J Nucl Med* 1995;36:37–44.
19. Even-Sapir E, Martin RH, Barnes DC, Pringle CR, Iles SE, Mitchell MJ. Role of SPECT in differentiating malignant from benign lesions in the lower thoracic and lumbar vertebrae. *Radiology* 1993;187:193–198.

Bone Marrow Scintigraphy Using Technetium-99m-Antigranulocyte Antibody in Hematologic Disorders

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Bone marrow is the primary site for many hematologic disorders. To date, however, no suitable bone marrow imaging method has been found. The present study investigates the usefulness of bone marrow immunoscintigraphy using ^{99m}Tc-labeled antigranulocyte antibody (anti-NCA-95) in 31 patients with hematologic disorders. **Methods:** One milligram of antibody labeled with 259-370 MBq ^{99m}Tc was injected intravenously, and bone marrow images were taken 4 hr later. We also calculated the uptake ratios of lumbar bone marrow-to-background (L/B) and ilium-to-background (I/B). **Results:** Of 15 patients with aplastic anemia, 7 showed diffusely decreased antibody uptake (L/B = 2.3 ± 0.8, I/B = 3.0 ± 0.8) compared to control patients (n = 21, L/B = 8.2 ± 2.5, I/B = 10.3 ± 3.1). Six patients had both decreased and increased uptake areas and two had normal to slightly increased uptake. Of those patients receiving various types of therapy for aplastic anemia, all but one showed increased or irregular uptake. The degree of antibody uptake in the bone marrow correlated with peripheral blood analyses (hemoglobin, white blood cells, platelets). Of six patients with myelodysplastic syndrome, four had irregular uptake and two diffusely decreased uptake. Four patients with myelogenous leukemia showed normal uptake, whereas two with lymphocytic leukemia had decreased uptake. Patients with iron deficiency anemia, pure red cell aplasia or thalassemia minor exhibited normal uptake with bone marrow expansion. **Conclusion:** Immunoscintigraphy with antigranulocyte antibody is a useful method for evaluating the bone marrow status of patients with various hematologic disorders.

Key Words: hematologic disorder; bone marrow scintigraphy; technetium-99m-anti-NCA-95; aplastic anemia; myelodysplastic syndrome

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Bone marrow disorders are the primary cause of many hematologic diseases. Aspiration and biopsy of the bone marrow have been used to evaluate patients, but these techniques are invasive, sometimes inadequate and do not accurately represent all the changes throughout the bone marrow tissue (*1,2*). Imaging bone marrow by whole-body scanning, using ^{99m}Tc-colloid, nanocolloid, ^{111}In-chloride, transferrin and radioiron, has been tried. Because of low radiopharmaceutical accumulation in the bone marrow and the poor physical characteristics of these radionuclides, bone marrow scintigraphy has thus far been unpopular (*3–7*).

Recently, a bone marrow scan using ^{99m}Tc-labeled antigranulocyte antibody, against nonspecific cross-reacting antigen-95, was developed (*8,9*). This immunoscintigraphic technique provides high-resolution bone marrow images and has been used clinically to diagnose marrow metastases (*10–12*). Potentially, it may be helpful in clinically assessing granulopoiesis or, more generally, hematopoiesis, but there have been few reports applying this technique to these diseases. In this preliminary study, we tested the clinical usefulness of bone marrow immunoscintigraphy in evaluating patients with hematologic disorders.

MATERIALS AND METHODS

Patients

We performed immunoscintigraphy on 31 patients (19 men, 12 women, aged 17–70 yr, mean age 38.9 yr), including 15 with aplastic anemia, 6 with myelodysplastic syndrome, 6 with acute leukemia and one each with iron deficiency anemia, pure red cell aplasia, thalassemia minor and Evan's syndrome (Table 1). We also performed bone marrow immunoscintigraphy in 21 control group patients with normal bone marrow function. These control patients had malignant diseases, and immunoscintigraphy was performed to evaluate marrow metastases.

Monoclonal Antibody

We used an in-house monoclonal antibody (CEA-79.4) directed against a nonspecific, cross-reacting antigen-95 (NCA-95), which is present in human granulopoietic cells (*9*). The antibody, which was generated using carcinoembryonic antigen (CEA) from LS174T cell supernatants (*13*), is an IgG_2a. Its recognized epitope is localized on CEA distinctive part and NCA-95. Its affinity constant is $2–9 \times 10^9$ liters/mole, and the number of antibody binding sites per granulocyte is $0.4–1.9 \times 10^5$ (*9*).

The antibody was labeled with ^{99m}Tc by a transchelation method using 2-mercaptoethanol (pH 5) as a reducing agent and glucarate as a ligand (*10*). The optimal labeling condition was an antibody to 2-mercaptoethanol molar ratio of 1:3000. The incubation time for labeling the antibody with ^{99m}Tc-labeled glucarate was 60 min. The labeling efficiency of CEA-79.4 with ^{99m}Tc was 60%–85%.

TABLE 1
Patient Distribution

Disorder	No. of patients
Aplastic anemia	15
Myelodysplastic syndrome	6
Acute leukemia	6
Myelogenous	4
Lymphocytic	2
Iron-deficiency anemia	1
Pure red cell aplasia	1
Thalassemia minor	1
Evan's syndrome	1
Total	31

Technetium-99m-labeled antibody was purified on a PD-10 column for immunoscintigraphy.

Several tests of the antibody's safety, including pyrogen testing and screens for the presence of bacteria, mycoplasma and viruses, were negative (*9*). Microbiological Associates Inc. (Rockville, MD), using the murine antibody production test, confirmed the safety of the CEA-79.4 antibody.

Scintigraphic Technique

Immunoscintigraphy was performed after obtaining informed consent from each patient. One milligram of antibody labeled with 259–370 MBq (5–10 mCi) ^{99m}Tc was injected intravenously for 5 min. Images were obtained 4 hr after injection. Whole-body and regional images were taken covering the entire hematopoietic marrow. Conventional whole-body and large field of view gamma cameras with high-resolution, low-energy collimators were used. An average of 400,000 counts were obtained. Additionally, we recorded posterior images of the lower lumbar region and pelvis on a dedicated computer. Regions of interest were selected over the lumbar vertebrae, ilium and soft-tissue background below the right kidney. We also calculated the uptake ratios of lumbar bone marrow-to-background (L/B) and ilium-to-background (I/B).

Statistical Analysis

Uptake ratio differences and peripheral blood findings in patients with aplastic anemia were tested for significance using Student's t-test. Values less than 0.05 were considered significant.

RESULTS

We grouped patients into three categories, those with "decreased," "irregular" and "normal or increased" uptake patterns. These categories were based on comparison with the control patients.

In evaluating the antigranulocyte antibody uptake pattern in aplastic anemia patients, we found that 7 of 15 patients had diffuse homogeneous decreased uptake throughout the entire marrow. Six patients had irregular uptake, i.e., a mixture of increased and decreased uptake areas. Two, however, had normal or slightly increased uptake. Seven patients with homogeneously decreased uptake showed significantly lower L/B and I/B ratios than control patients (Table 2). Immunoscintigraphy was done before treatment in seven patients, and after treatment in eight. Studies were not repeated in these patients. We compared the uptake pattern with the treatment received by the patients. Six patients with decreased uptake and one with irregular uptake underwent immunoscintigraphy before treatment. Of eight patients who received therapy, such as oxymetholon, GM-CSF or antilymphocyte globulin, one had decreased uptake, five had irregular heterogeneous uptake and two had normal to slightly increased uptake (Table 3). One patient with decreased uptake received steroid therapy for 1 mo prior to scintigraphy. The others had been medicated for periods of 8 mo to 5 yr.

TABLE 2
Antibody Uptake Ratio in Aplastic Anemia Patients with Decreased Marrow Uptake

Ratio	Aplastic anemia (n = 7)	Control (n = 21)
L/B	2.3 ± 0.8*	8.2 ± 2.5*
I/B	3.0 ± 0.8†	10.3 ± 3.1†

*†$p < 0.001$.

Mean ± s.d. is shown. L/B = lumbar spine-to-background; I/B = ilium-to-background.

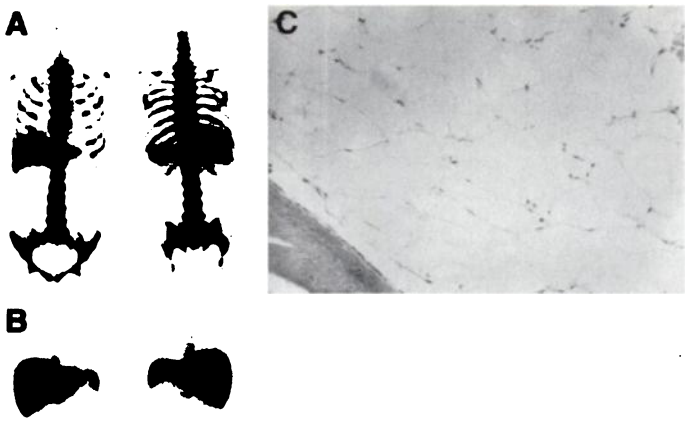

FIGURE 1. Anterior and posterior whole-body images in a normal volunteer (A) and a patient with aplastic anemia (B). Compared to the normal patient, the one with aplastic anemia had homogeneously decreased antibody uptake. Blood levels of hemoglobin, WBC and platelet were 6.6 g/dl, 2000/mm^3 and 17,000/mm^3, respectively. Bone marrow biopsy exhibited markedly decreased cellularity (C).

Figure 1A shows a whole-body image of a normal volunteer. Figure 1B shows an aplastic anemia patient with diffuse low antibody uptake in the bone marrow compared to the normal patient. This patient's bone marrow biopsy revealed that many portions of the marrow were replaced by fatty tissues, with a cellularity of 10% (Fig. 1C). Figure 2 depicts irregular uptake in an aplastic anemia patient, with both decreased and increased uptake areas. Figure 3 shows slightly increased uptake in the bone marrow of an aplastic anemia patient who took oxymetholon for 9 mo prior to the study. Homogeneous increased antibody uptake was discerned.

Table 3 shows peripheral blood analysis results for the three groups of patients. There was little difference between the group with decreased uptake and the one with irregular uptake. The two patients with normal or increased uptake had higher hemoglobin levels.

In evaluating the uptake pattern in myelodysplastic syndrome patients, we observed that four had heterogeneous antibody uptake, i.e., a mixture of increased or normal and decreased uptakes. Two patients had diffuse decreased uptake, but one also had myelofibrosis and the other was in remission following chemotherapy.

Figure 4 presents a posterior image of the vertebra of a patient with myelodysplastic syndrome. Both increased or normal uptake and decreased uptake of the antibody was detected. Alkaline phosphatase anti-alkaline phosphatase staining of bone marrow obtained from biopsy showed a large number of blasts, which were not taken up by antibody (*9*).

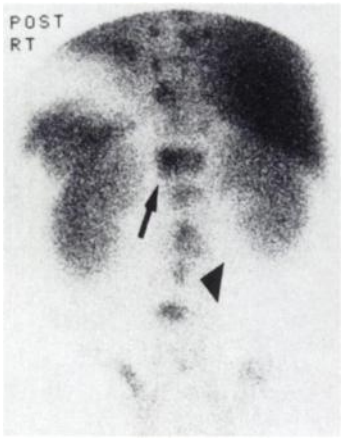

FIGURE 2. Posterior image of the vertebra of an aplastic anemia patient. Irregular antibody uptake can be seen in the bone marrow.

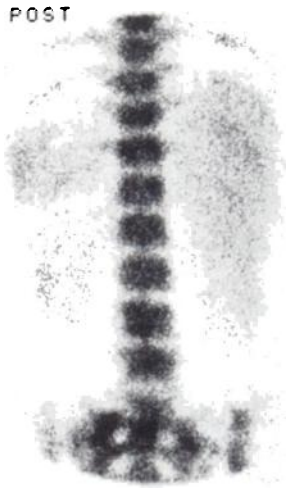

FIGURE 3. Posterior image of the vertebra of an aplastic anemia patient after oxymetholon therapy. Diffusely increased bone marrow uptake can be seen.

Four patients with myelogenous leukemia had normal or increased uptake with bone marrow expansion, but two patients with lymphocytic leukemia showed almost no antibody uptake in the bone marrow. Figure 5, a posterior image of a patient with acute myelogenous leukemia, shows normal antibody uptake in the vertebra but increased uptake in the spleen which might be due to leukemic infiltration. Figure 6, a posterior image of a patient with acute lymphocytic leukemia, reveals markedly low antibody uptake throughout the entire marrow.

Bone marrow scintigraphy in patients with iron-deficiency anemia, pure red cell aplasia and thalassemia minor showed normal uptake with marrow expansion (Fig. 7). Scintigraphy in an Evan's syndrome patient with thrombocytopenia and anemia showed decreased uptake with marrow expansion (data not shown).

DISCUSSION

Peripheral blood analysis, bone marrow examination and other nonscintigraphic procedures usually provide adequate information to accurately diagnose and effectively manage most hematologic disorders (*1*). Bone marrow aspiration and biopsy, however, are susceptible to sampling error, especially in patients with nonuniform marrow. In addition, bone marrow biopsy is invasive and cannot fully represent changes throughout the entire tissue (*2*).

Bone marrow scintigraphy has been developed to solve these problems. It is capable of imaging three types of cells: (a) erythropoietic precursor cells, (b) reticuloendothelial system (RES) cells and (c) granulopoietic cells. ^{52}Fe and ^{59}Fe are used for erythropoietic marrow imaging and ^{99m}Tc-colloid for RES imaging. The end target cells of ^{111}In have not been identified,

TABLE 3
Peripheral Blood Analyses Compared with Bone Marrow Scintigraphy Results in Aplastic Anemia Patients

Pattern	Treatment* Before	Treatment* After	Hb (g/dl)	WBC (×10^3/mm^3)	Platelet (×10^3/mm^3)
Decreased uptake	6	1†	7.6 ± 2.8	3.0 ± 1.4	23 ± 20
Irregular uptake	1	5	7.0 ± 2.0	3.2 ± 1.6	24 ± 11
Normal or increased uptake	0	2	10.2 ± 1.7	3.8 ± 0.1	31 ± 7

*Oxymetholon, GM-CSF, antilymphocyte globulin.
†Therapy for 1 mo.
Mean ± s.d. is shown.

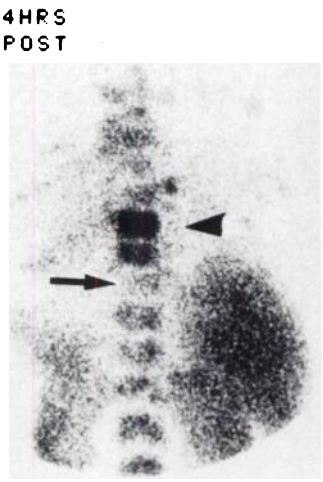

FIGURE 4. Posterior image of the vertebra in a myelodysplastic syndrome patient. Increased uptake (arrowhead) and decreased uptake (arrow) of the antibody can be seen together.

but it has been hypothesized that it targets erythropoietic marrow (*14,15*).

RES imaging agents are popular, but there may be a discrepancy between the locations of RES marrow and hematopoietic elements in hematologic disease (*16*). Because a small amount of ^{99m}Tc-colloid accumulates in the red marrow, compared to the liver and spleen, obtaining a suitable marrow image is difficult. In cases of radioiron, ^{59}Fe requires special high-energy collimators, and ^{52}Fe has a positron emission. Because of poor physical characteristics, these radioiron isotopes cannot be applied clinically. Using ^{111}In-chloride as an iron substitute has not proven satisfactory. Although ionic indium behaves similarly to iron by sharing the transferrin transport system, there are significant quantitative differences (*17,18*). Finally, ^{111}In-chloride's high cost and relatively poor imaging qualities also contribute to its unpopularity as an imaging agent.

Technetium-99m-labeled murine monoclonal antibodies were recently developed for tagging patient granulopoietic cells in vivo (*8,19*). Of particular interest is ^{99m}Tc-labeled antibody against NCA-95, which is expressed in the cytoplasm and cell membrane of granulopoietic cells and has been developed to image infection and bone marrow (*9–11*). High-quality, whole-body imaging of granulopoietic or, more generally, hematopoietic marrow, is now routinely possible in the clinical setting. The ultimate potential of quantitative bone marrow scanning to assess specific aspects of human granulopoiesis has not been fully elucidated (*20*).

Aplastic anemia is a life-threatening hematologic disorder characterized by pancytopenia and bone marrow hypoplasia. Before treatment, all but one of the patients in our study showed homogeneously decreased uptake of anti-NCA-95 antibody in

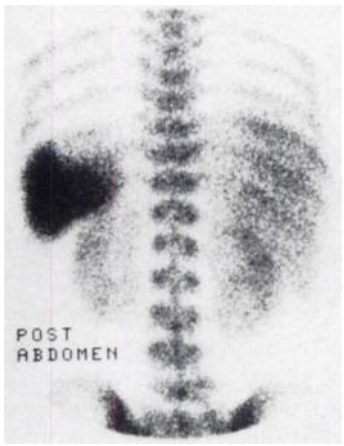

FIGURE 5. Posterior image of the vertebra in an acute myelogenous leukemia patient shows a normal uptake pattern.

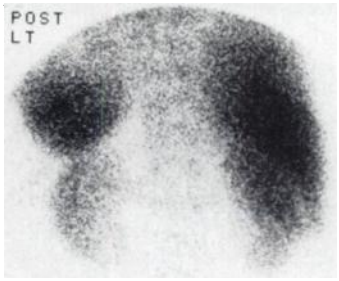

FIGURE 6. Posterior image of the vertebra of an acute lymphocytic leukemia patient shows markedly decreased uptake.

the hematopoietic marrow. Similar observations have been reported by other investigators using ^{99m}Tc-colloid (*2,16*) and ^{111}In-chloride (*17,21,22*). We found increased uptake in two medicated patients. Interestingly, heterogeneous uptake was observed in five patients during or after treatment. Infection or metastasis of the bone and/or marrow causes increased or heterogeneous antibody uptake, but there was no such case in this study. Hotta et al. (*23*) reported a similar finding and suggested that bone marrow regeneration occurs in restricted areas. It is unclear why patchy hematopoiesis persists in aplastic anemia. It seems likely that damage to the bone marrow microenvironment plays an important role in the disorder's pathophysiology (*23,24*). Peripheral blood analyses did not differ between the groups with decreased and irregular uptake. Padhy et al. (*2*) found that improved bone marrow topography and uptake index due to treatment occur much earlier than any appreciable change in bone marrow cellularity or peripheral blood analyses. Therefore, marrow imaging may be more sensitive than conventional methods in detecting early changes in bone marrow function following treatment. In two cases of normal or increased marrow uptake, hemoglobin levels improved more than WBC or platelet counts. This is concordant with the finding that erythroid recovery precedes that of granulocytes and platelets in androgen-treated patients (*21*). Possibly, the amount and distribution of anti-NCA-95 taken up by the marrow gives a prognosis similar to that obtained using ^{111}In-chloride (*15*).

Myelodysplastic syndromes are characterized by ineffective hematopoiesis or increased intramedullary destruction of mature hematopoietic cells. Four patients with myelodysplastic syndrome showed heterogeneous antibody uptake, with both decreased and increased uptake areas. Reske (*25*) reported similar findings. Accumulation of blasts to which the antibody does not bind might cause the small focal defects in the marrow

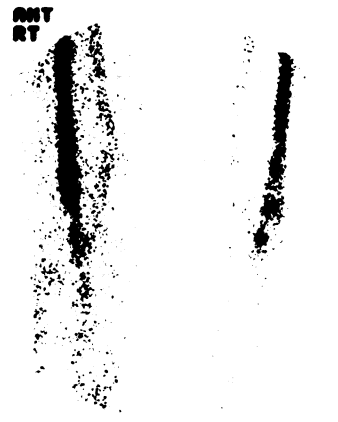

FIGURE 7. Anterior image of the femur of an iron-deficiency anemia patient shows bone marrow expansion of the femur around the knee.

immunoscintigraphy. Tricot et al. (*26*) described the dislocation of immature granulopoietic cells during myelodysplastic syndrome, including blasts in the bone marrow, as an abnormal localization of immature precursors (ALIP). They also reported that ALIP is an adverse prognostic finding that is very accurate in predicting which patients will have a short survival time and which will have early transformation to acute leukemia (*26,27*). We expect that the immunoscintigraphic technique described here can provide useful information to diagnose and classify this complex syndrome.

In the myelogenous leukemia patients, myelocytes expressed NCA-95 to a variable degree, and normal or increased uptake of the anti-NCA-95 antibody was observed in all four patients. Of course, because of the lack of lymphoid cell binding sites, there was markedly decreased uptake in acute lymphocytic leukemia subjects.

In patients with other disorders, such as iron deficiency anemia, pure red cell aplasia, thalassemia minor and Evan's syndrome, immunoscintigraphy revealed bone marrow expansion. Peripheral bone marrow expansion can also be evaluated with bone-seeking radiopharmaceuticals (*1*). Findings of marrow expansion in ^{99m}Tc-labeled phosphate bone scans are not specific or clear. In comparison, the immunoscintigraphy protocol described in this article provides more precise images and can be used to evaluate bone marrow functional states.

CONCLUSION

Until now, immunoscintigraphy with antigranulocyte antibody has been used to detect bone marrow metastasis and to localize inflammation (*10,11,28,29*). This preliminary report suggests that it may also be effectively used to evaluate the functional status of bone marrow during disease and treatment.

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REFERENCES

1. Fordham EW, Ali A. Radionuclide imaging of bone marrow. *Semin Hematol* 1981;18:222–239.
2. Padhy AK, Garg A, Kochupillai V, Gopinath PG, Basu AK. Marrow uptake index: a quantitative scintigraphic study of bone marrow in aplastic anemia. *Thymus* 1987;10: 137–146.
3. Greenberg ML, Atkins HL, Schiffer LM. Erythropoietic and reticuloendothelial function in bone marrow in dogs. *Science* 1966;152:526–528.
4. Farrer PA, Saha GB, Kalz M. Further observation of the use of indium 111-transferrin for the visualization of bone marrow in man. *J Nucl Med* 1973;14:394–395.
5. McNeil BJ, Holman BL, Button LN, et al. Use of indium-chloride scintigraphy in patients with myelofibrosis. *J Nucl Med* 1974;15:647–651.
6. Chaudhri TK, Ehrhardt JC, DeGowin RL, et al. Ferrous-59 whole-body scanning. *J Nucl Med* 1974;15:667–673.
7. Knospe WH, Rayudu GV, Cardello M, et al. Bone marrow scanning with iron-52. Regeneration and extension of marrow after ablative doses of radiotherapy. *Cancer* 1976;37:1432–1442.
8. Steinstraesser A, Schorlemmer HU, Schwarz A, Kuhlmann L, Bosslet K. A novel ^{99m}Tc-labeled antibody for in vivo targeting of granulocyte. *J Nucl Med* 1988;29:925.
9. Choi CW, Chung J-K, Lee DS, Lee MC, Chung H-K, Koh C-S. Development of bone marrow immunoscintigraphy using a ^{99m}Tc-labeled anti-NCA-95 monoclonal antibody. *Nucl Med Biol* 1995;22:117–123.
10. Reske SN, Karstens JH, Gloeckner MW, Schwarz A, Steinstraesser A, Ammon J, Buell U. Radioimmunoimaging of bone marrow. Results in patients with breast cancer and skeletal metastases and patients with malignant melanoma. *Lancet* 1989;2:299–301.
11. Duncker CM, Carrio I, Berna L, et al. Radioimmune imaging of bone marrow in patients with suspected bone metastases from primary breast cancer. *J Nucl Med* 1990;31:1450–1455.
12. Lee KH, Choi CW, Bang YJ, et al. Bone marrow immunoscintigraphy for the detection of skeletal metastases in malignant tumors: a comparison with ^{99m}Tc-MDP bone scan. *Kor J Nucl Med* 1994;28:89–97.
13. Lee J-H, Chung H-K, Kimm S-W. Purification of carcinoembryonic antigen from culture supernatant of human colon cancer cell line LS174T using monoclonal immunoaffinity chromatography. *Kor J Biochem* 1988;20:23–32.
14. Lilien DL, Berger HG, Anderson DP, et al. Indium-111-chloride: a new agent for bone marrow imaging. *J Nucl Med* 1973;14:184–186.
15. McNeil BJ, Rappeport JM, Nathan DG. Indium chloride scintigraphy: an index of severity in patients with aplastic anemia. *Br J Haematol* 1976;34:599–604.
16. Mishkin FS, Freeman LM. Miscellaneous applications of radionuclide imaging. In: Freeman LM. ed. *Freeman and Johnson's clinical radionuclide imaging,* 3rd ed. Orlando: Grune & Stratton; 1984:1365–1460.
17. McIntyre RA, Larson SM, Scheffel U, et al. Comparisons of metabolism of iron-transferrin and indium-transferrin by erythropoietic marrow. *J Nucl Med* 1973; 14:425–426.
18. Staub RF, Gorston E. Indium-111-chloride distribution kinetics in hematologic disease. *J Nucl Med* 1973;14:456–457.
19. Joseph K, Hoeffken H, Bosslet K, Schorlemmer HU. In vivo labeling of granulocytes with ^{99m}Tc anti-NCA monoclonal antibodies for imaging inflammation. *Eur J Nucl Med* 1988;14:367–373.
20. Berna L, Germa JR, Estorch M, Torres G, Blanco R, Carrio I. Bone marrow regeneration after hormonal therapy in patients with bone metastases from prostate carcinoma. *J Nucl Med* 1991;32:2295–2298.
21. Najean Y, Le Danvic M, Le Mercier N, Pecking A, Colonna P, Rain JD. Significance of bone marrow scintigraphy in aplastic anemia: concise communication. *J Nucl Med* 1980;21:213–218.
22. Sayle BA, Helmer III RE, Birdsong BA, Balachandran S, Gardner FH. Bone marrow imaging with indium-111-chloride in aplastic anemia and myelofibrosis: concise communication. *J Nucl Med* 1982;23:121–125.
23. Hotta T, Murate T, Inuoe C, et al. Patchy haemopoiesis in long-term remission of idiopathic aplastic anemia. *Eur J Haematol* 1990;45:73–77.
24. Gordon MY, Gordon-Simth EC. Bone marrow fibroblastoid colony-forming cells (F-CFC) in aplastic anemia: colony growth and stimulation of granulocyte-macrophage colony forming cells (GM-CFC). *Br J Haematol* 1981;49:465–477.
25. Reske SN. Recent advances in bone marrow scanning. *Eur J Nucl Med* 1991;18:203–221.
26. Tricot G, Do Wolf-Peeters C, Vlietinck R, et al. Bone marrow histology in myelodysplastic syndromes: II. Prognostic value of abnormal localization of immature precursors in MDS. *Br J Haematol* 1984;58:217–225.
27. Tricot G, Vlietinck R, Verwilghen RL. Prognostic factors in the myelodysplastic syndromes: a review. *Scand J Haematol* 1986;36 (suppl 45):107–113.
28. Locher JT, Seybold RY, Andres PA, Schubiger JP, Mach F. Imaging of inflammatory and infectious lesions after injection of radioiodinated monoclonal anti-granulocyte antibodies. *Nucl Med Commun* 1986;7:659–670.
29. Seybold K, Locher JT, Coosemans C, et al. Immunoscintigraphic localization of inflammatory lesions: clinical experience. *Eur J Nucl Med* 1988;13:587–593

EDITORIAL

Noninvasive Evaluation of the Bone Marrow

The study reported by Chung et al. (*1*) in this issue reflects the evolution of sophisticated, noninvasive technology for the evaluation of bone marrow anatomy, function and disease. Such methods offer the major advantage of visualizing the entire marrow, or at least a major portion of the bone marrow, as compared to the small sampling obtained by bone marrow aspiration and biopsy. Each of these new technologies, however, has its own shortcomings that limit it as a sole method of studying the marrow. Such methods alone are not likely to replace bone marrow aspiration or biopsy and pathologic review. In combination, however, they may offer complementary information to the aspirate and biopsy and to each other, and help to improve patient management. There are two major methods of noninvasively studying the

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