Disseminated Bone Marrow Metastases from Primary Breast Cancer: Detection and Follow-up by Radioimmune Bone Marrow Scintigraphy

Olaf Rieker, Frank Grünwald, Günter Layer, Christian M. Kurbacher, Andreas L. Hotze, Christian Menzel and Hans J. Biersack

Departments of Nuclear Medicine, Radiology and Gynecology, University of Bonn, Bonn, Germany

Bone scintigraphy of a 40-yr-old patient suffering from primary breast cancer suggested the possibility of diffuse metastases. Bone marrow scintigraphy using ^{99m}Tc-labeled monoclonal antibodies (BW 250/183) demonstrated diffuse destruction of bone marrow due to metastatic disease and consecutive bone marrow extension. Bone marrow scintigraphy was highly sensitive in detecting progression of disease in this asymptomatic patient.

Key Words: bone marrow scintigraphy; repeat immunoscans; disseminated metastases; follow-up

J Nucl Med 1994; 35:1485–1487

Bone scans, although highly sensitive in the detection of bone metastases, may underestimate bone marrow involvement. Bone marrow scintigraphy, using the ^{99m}Tc-labeled monoclonal antibody BW 250/183, was able to detect more lesions than bone scintigraphy in cases with metastatic disease (*1–3*).

We present a case where total-body bone marrow scintigraphy was useful in evaluating progressive bone marrow destruction and extension in a patient without clinical symptoms.

CASE REPORT

A 40-yr-old woman underwent mastectomy because of right-sided breast carcinoma. Adnectomy and hysterectomy were performed because of additional ovarian tumor. Histology detected invasive, partly ductal, partly lobular carcinoma of the breast (pT_4, pN_2) and ovarian metastasis. Adjuvant chemotherapy was initiated. No radiation therapy was performed. Except for moderate anemia (Hb: 122 g/liter) and slightly elevated erythrocyte sedimentation rate (ESR) (13 mm/hr), laboratory tests were normal. The chest radiograph showed sclerosis of the vertebral column.

Received Aug. 18, 1993; revision accepted May 5, 1994.

For correspondence or reprints contact: Olaf Rieker, MD, Clinic for Nuclear Medicine, University of Bonn, Sigmund-Freud-Str. 25, 53127 Bonn, Germany.

The bone scan demonstrated increased uptake of ^{99m}Tc-MDP in skull, proximal humeri, distal femora and proximal tibiae (Fig. 1). A discrete posterior lesion was found in a rib.

A whole-body bone marrow scan was performed 4 hr after injection of 555 MBq (15 mCi) ^{99m}Tc-labeled monoclonal antibody BW 250/183 (Behringwerke AG, 6230 Frankfurt, FRG).

This tracer visualizes the hematopoietic bone marrow by labeling granulocytes and myelocytes. The bone marrow scan revealed nearly complete destruction of central bone marrow

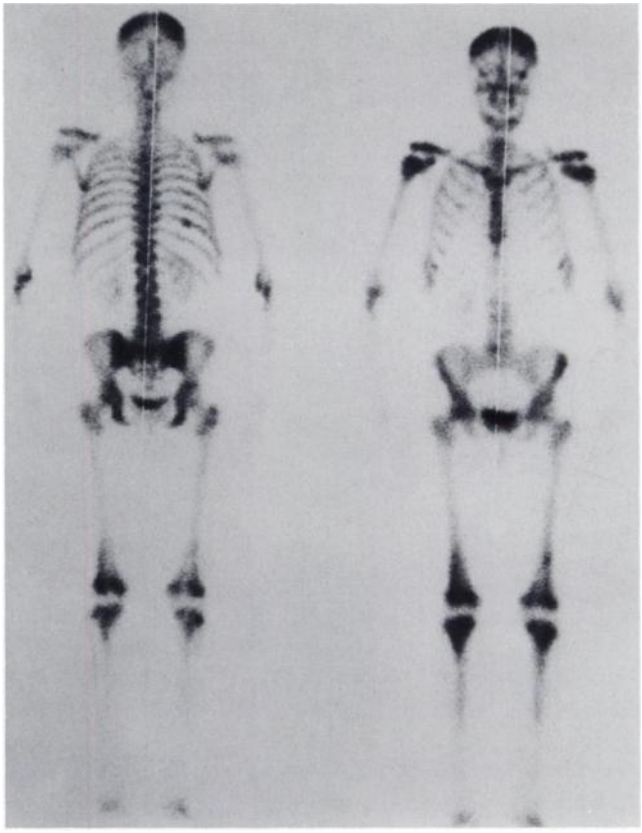

FIGURE 1. Anterior and posterior bone scan (^{99m}Tc-MDP) of a patient suffering from breast cancer shows increased uptake in the calvaria, proximal humeri, distal femora and proximal tibiae. Except for posterior part of rib IX, discrete lesions are not clearly visualized.

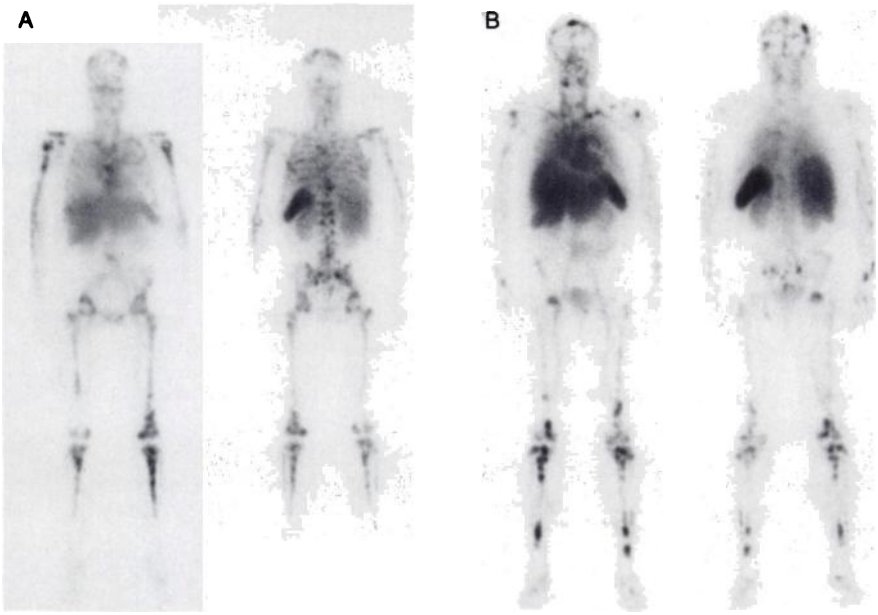

FIGURE 2. (A) Anterior and posterior bone marrow scans acquired 4 hr after injection of ^{99m}Tc-labeled antibody BW 250/183 showing destruction of the central marrow and extension to peripheral bones (humeri, femora, tibiae). Only residual bone marrow is visible in ribs and spine. (B) Repeated bone marrow scan 18 mo later. Bone marrow in ribs, vertebral column, pelvic bones and major parts of the extremities has been completely displaced. Previously extended marrow in the tibiae is now also involved.

and extension of bone marrow as far as to the cubital region and tibiae (Fig. 2A). Unexpected accumulation of tracer was visualized in the liver, potentially due to extramedullary hematopoiesis.

MRI of the spine showed an inhomogeneous decrease of signal intensity in all vertebral bodies, confirming diffuse metastatic spread to the vertebral bone marrow (Fig. 3A). Therapy was changed from tamoxifene 30 mg daily to medroxyprogesterone acetate 1000 mg daily.

Eighteen months later, examinations were repeated since ESR and serum CA 15-3 were elevated. While Hb (114 g/liter) and thrombocytes (104.000/μl) were decreased, the leucocyte count and all other parameters were within normal ranges. HAMA was found to be slightly elevated.The patient still felt well and did not have any complaints of skeletal pain or discomfort. Chest radiograph excluded pulmonary metastases. Ultrasound and computed tomography of the abdomen ruled out liver metastases. The bone scan was unchanged compared to the previous study. Bone marrow scintigraphy disclosed progression of central bone marrow destruction and further marrow extension (Fig. 2B). Previously expanded bone marrow in humeri and femora was no longer visualized, indicating progressive metastatic involvement. Liver uptake was increased possibly due to the development of HAMA following the first infusion of the antibody.

Repeated MRI of the spine (24-mo interval) showed a more homogeneous decrease of signal intensity, consisting with progression of the disease (Fig. 3B). In order to prevent further progression, low-dose chemotherapy was started (epirubicine, 30 mg/wk).

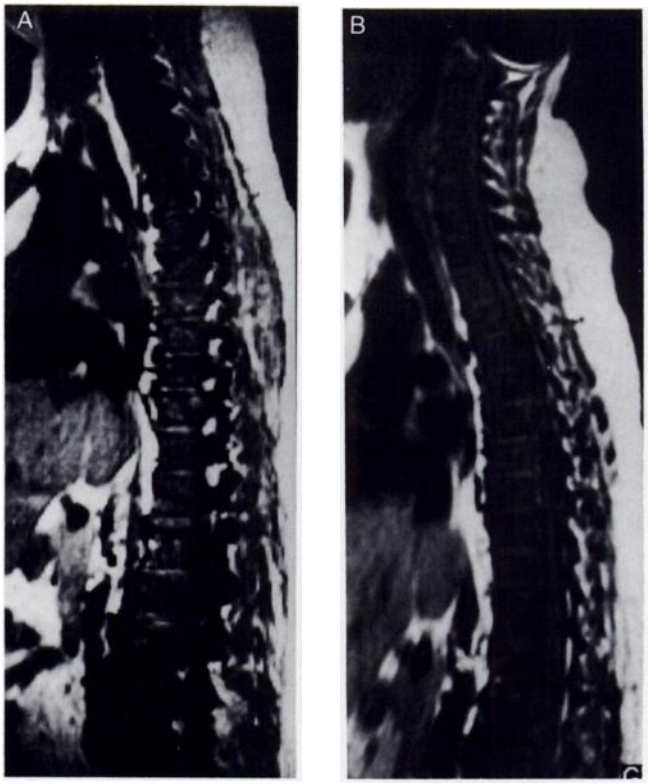

FIGURE 3. (A) MRI of the spine. T1-weighted sagittal sections. Inhomogeneous decrease of signal intensity in all vertebral bodies, due to replacement of fatty bone marrow by diffuse metastases. (B) Repeated MRI of the spine 24 mo later (parameters of acquisition unchanged). Homogeneous decrease of signal intensity is observed in all vertebral bodies, indicating progressive bone marrow involvement.

DISCUSSION

It is well known that diffuse bone marrow metastases may occasionally be missed in radiographs or may be mis-

taken for osteoporosis (*4*). Bone scans in diffuse bone marrow involvement can result in a generalized increase of uptake, lacking focal lesions (*5–7*). "Superscans" are frequently found in diffuse skeletal spread of prostatic cancer. Absent visualization of the kidneys is an important criterion in this case (*5*). Later, it was reported that there was increased tracer uptake in the ends of long bones (humeri, femura) which is also a characteristic feature (*7*). Bone marrow scintigraphy using ^{99m}Tc-labeled monoclonal antibodies directed against granulocytes and myelocytes is superior to radiocolloid scans since there is only low liver uptake in normals (*1,8,9*). In this patient, abnormal liver uptake was seen, potentially due to extramedullary hematopoiesis or to the development of human anti-murine antibodies (HAMA). HAMAs were slightly elevated in this patient following the repeated administration of the antibody. In rare cases we have observed that HAMA prevented "immunoscanning." No tracer uptake in the bone marrow was visible in these cases, however, the extension of hematopoietic bone marrow and the development of further defects in previously extended bone marrow cannot be mimicked by HAMAs.

In our patient, immunoscintigraphy of the bone marrow elucidated an uncommon bone scan. A repeated bone marrow scan was a very sensitive technique to demonstrate progression of metastatic disease.

If bone scans and radiographs are inconclusive for diffuse skeletal metastases, bone marrow scintigraphy will give the definite diagnosis. In the follow-up of diffuse metastatic disease, whole-body bone marrow scans are highly sensitive in the detection of a stepwise progression. Bone marrow "immunoscan" is able to replace MRI and bone scintigraphy in therapy control of disseminated metastases of primary breast cancer.

REFERENCES

1. Duncker CM, Carrió I, Berná 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.
2. Reske SN, Karstens JH, Gloeckner W, et al. Radioimmunoimaging of bone marrow involvement in breast cancer and malignant lymphoma. *Lancet* 1989;i:299–301.
3. Reske SN. Recent advances in bone marrow scanning. *Eur J Nucl Med* 1991;118:203–221.
4. Rankin S. Radiology. In: Rubens RD, Fogelman I, eds. *Bone metastases*. London: Springer-Verlag; 1991:63–81.
5. Fogelman I, McKillop JH, Greig WR, Boyle IT. Absent kidney sign associated with symmetrical and uniformly increased uptake of tracer by the skeleton. *Eur J Nucl Med* 1977;2:257–260.
6. Fogelman I, Maisey M. *An atlas of clinical nuclear medicine*. London: Martin Dunitz Ltd; 1988:18–20.
7. Fogelman I, McKillop JH. The bone scan in metastatic disease. In: Rubens RD, Fogelman I, eds. *Bone metastases*. London: Springer-Verlag; 1991;31–61.
8. Munz DL, Sandrock D, Rilinger N. Comparison of immunoscintigraphy and colloid scintigraphy of bone marrow. *Lancet* 1990:i:258.
9. Hugget SM, Nimalaraj TH, Costa DC, Ell PJ. Nanocolloid imaging in early bone or marrow metastatic spread out. *J Nucl Med Technol* 1991;19: 33–35.