Acute Effects of Radiation Therapy on Indium-111-Labeled Leukocyte Uptake in Bone Marrow

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We recently performed [^{99m}Tc]MDP bone and ^{111}In-labeled leukocyte scintigraphy on a patient receiving radiation therapy to the lower cervical and upper thoracic spine. While the bone images revealed only minimally increased activity in the radiation port, leukocyte images revealed diffuse, intensely increased uptake in this same region. Radiation therapy should be included in the differential diagnosis of increased bone marrow activity on ^{111}In leukocyte images.

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The early or acute effects of radiation therapy on uptake of the technetium-99m- (^{99m}Tc) labeled bone agents by irradiated bone range from no change to increased radiotracer accumulation (*1,2*).

Indium-111- (^{111}In) labeled leukocyte (WBC) scintigraphy is a sensitive, specific method for investigation of infection (*3*). The normal distribution of the labeled leukocytes is limited to liver, spleen and bone marrow (*4,5*). Reports of osseous localization of leukocytes in the absence of infection include neoplasm and recent fracture (*6–11*). While diminished labeled leukocyte uptake in bone marrow as a late consequence of previous external radiation therapy has been described (*12*), we recently encountered intense diffusely increased leukocyte accumulation in the lower cervical and upper thoracic spine of a patient undergoing radiation therapy to this region at the time scintigraphy was performed. This case suggests that, at least acutely, radiotherapy causes increased bone marrow activity on WBC images.

CASE REPORT

A 66-yr-old female who had undergone a radical vulvectomy for squamous cell carcinoma of the vulva 15 mo prior, presented at our institution with a 1-mo history of severe right shoulder pain. A right paravertebral mass along the upper thoracic spine was present on chest x-ray. Computed tomography revealed partial destruction of the second thoracic vertebra, as well as cervical extension of the paravertebral mass. The diagnosis was that of metastatic vulvar carcinoma and the patient underwent technetium-99m (^{99m}Tc) methylene diphosphonate bone (MDP) scintigraphy as part of a metastatic evaluation. Forty-eight hours after completion of MDP imaging, the patient underwent WBC scintigraphy because of the sudden onset of rigors and fever to 39°C. Imaging was performed 24 hr after injection of 18.5 mBq (500 μCi) of autologous leukocytes, labeled with [^{111}In]oxine according to the method of Thakur et al. (*3*). Both MDP and WBC images revealed photopenic defects in the second thoracic vertebra and a portion of the second right posterior rib. Minimally increased activity in the lower cervical and upper thoracic spine was noted on MDP images (only in retrospect) while a rectangular area of intensely increased activity extending from the lower cervical to the mid thoracic spine, including multiple left costovertebral articulations and the medial aspect of several right posterior ribs, was evident on WBC images (Fig. 1).

The patient was receiving fractionated radiation therapy, from a 4MV linear accelerator, to a port measuring 9 cm × 17 cm extending from the fourth cervical vertebra to the sixth thoracic vertebra, and corresponding to the area of increased tracer activity noted on the radionuclide images (Fig. 2). At the time of MDP imaging the patient had received 2000R; her most recent treatment (250R) was administered after radiopharmaceutical injection and before imaging; she received no additional radiation therapy prior to WBC scintigraphy.

DISCUSSION

The acute effects of ionizing radiation on bone are twofold: increased cell membrane permeability with

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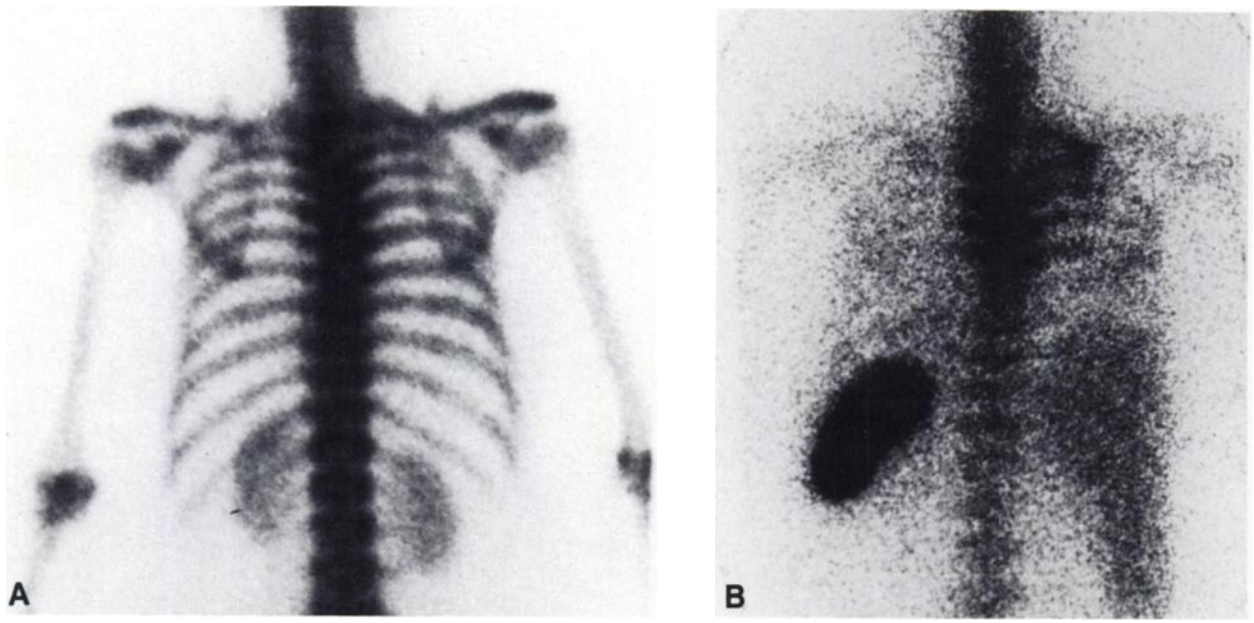

FIGURE 1
A: Posterior 3-hr MDP image. There is minimally increased activity in the lower cervical and upper thoracic spine. A photopenic defect involving T2 and part of the second right posterior rib is evident. B: Posterior 24-hr WBC image. There is intense activity in the lower cervical and upper thoracic spine as well as the corresponding left costovertebral articulations. Increased activity in the medial aspect of the first and the third through the sixth posterior ribs on the right is also present. A photopenic defect involving T2 and part of the second right rib posteriorly, similar to that on the MDP images, is noted.

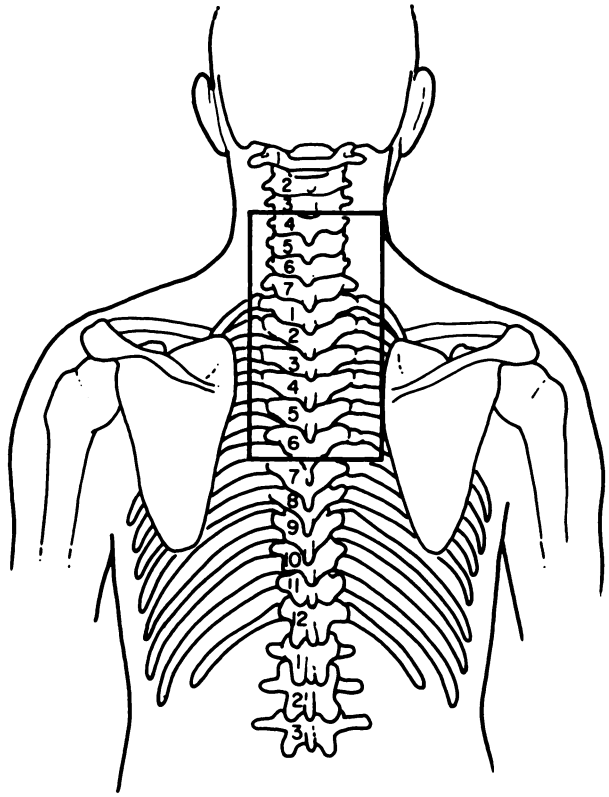

FIGURE 2
Diagram of the radiation port.

transudation of plasma through the endothelium into the vessel walls producing edema, and an inflammatory response secondary to granulocyte infiltration of vessel endothelium (*13*). Ionizing radiation has additional effects on bone marrow: shrinkage of marrow parenchyma, as a result of hematopoietic cell destruction, and an increase in the sinusoidal blood volume of the marrow. At exposures of 1500R or more the sinusoids may expand to the point of rupture, with resultant hemorrhage into the marrow parenchyma (*14*).

At the time this patient underwent radionuclide imaging, she had received a total of 2000R, sufficient to produce increased cell membrane permeability, granulocyte infiltration of the vessel walls, and increased marrow blood volume. The disparity between WBC and MDP images is, presumably, a reflection of the relative radiosensitivity of the tissues imaged with each procedure. Hematopoietic tissue and fine vascular tissue are much more radiosensitive than mature bone (*15*). It has been demonstrated in animals that, at 24 hr after an exposure of 1750 rad, tracer uptake by bone increases ~20% (*1*) while at 24 hr after an exposure of 1500–1750 R, marrow blood volume increases between 175%–214% (*1,14*).

The subtle findings on the MDP images reflect the mild increase in radiotracer uptake by bone. The WBC images probably reflect a combination of increased marrow blood volume, as well as granulocyte infiltra-

tion of vessel walls. The striking difference between these two images provides a visual and clinical correlate to the disparate acute effects of external radiation on bone and bone marrow, which have been described in animals.

Radiation therapy, at least initially, results in increased bone marrow uptake of labeled leukocytes. The pattern of intense, diffusely increased bone marrow activity on WBC images corresponding to a radiation port, combined with appropriate clinical history, should facilitate its recognition.

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