

Flare Phenomenon in Osteosarcoma after Complete Remission

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A patient undergoing cytostatic therapy for osteosarcoma of the right humerus had bone scans at 2-mo intervals. A skeletal focus of increased radiotracer accumulation occurred and subsequently was confirmed by CT and MRI. A necrotic metastasis was found during biopsy. There were no remaining viable tumor cells. This finding confirms the presence of the flare phenomenon in skeletal metastases in primary malignant bone tumors and that radionuclide imaging may fail to detect intramedullary foci of viable metastases in these tumors.

Key Words: osteosarcoma; flare phenomenon; computed tomography; magnetic resonance imaging; remission

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Flare responses on bone imaging have been well documented in patients with breast and prostatic carcinoma (1,2) and, to a lesser extent, in other tumors such as small-cell carcinoma of the lung (3). It is characterized by increased tracer accumulation on bone scans in metastatic foci of the skeleton after the start of systemic therapy, despite clinical improvement (4). The reports on the flare phenomenon are scarce for other tumor types. One report includes histologic correlation of primary malignant bone tumors with soft-tissue manifestation of flare (5,6).

CASE REPORT

A 17-yr-old boy presented with a 4-mo history of pain in the right upper arm. Diagnostic evaluation with CT and fine-needle aspiration biopsy revealed an osteosarcoma in the right proximal humerus. Preoperative cytostatic treatment was given for 8 wk. Amputation of the right arm through the scapular neck was subsequently performed.

At the initial bone scan, extensive tracer accumulation was found in the primary tumor proximally in the right humerus. There was also a small area of tracer accumulation in the right pubic bone that was initially overlooked (Fig. 1).

A follow-up scan 2 mo later, near the completion of the initial cytostatic treatment, revealed additional faint isotopic accumulation in the mid-diaphyseal area of the right femur (Fig. 2). Conventional x-ray examination of the femur was normal, whereas CT showed increased density of the medullary cavity of the right

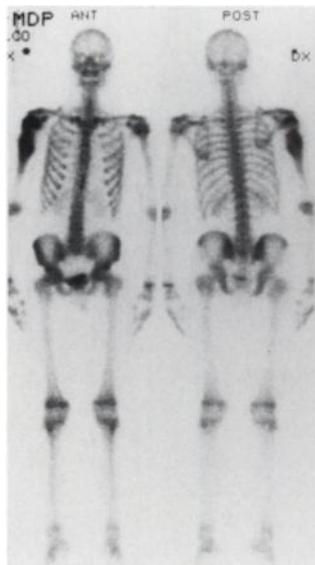


FIGURE 1. Initial bone scan demonstrates intense tracer uptake at the site of the primary tumor in the proximal portion of the right humerus. A small area of radiotracer accumulation medially in the right pubic bone was initially overlooked due to its close proximity to the urinary bladder. A small accumulation in the right part of the fifth lumbar vertebra is also seen but was not confirmed to represent metastatic disease on subsequent examinations.

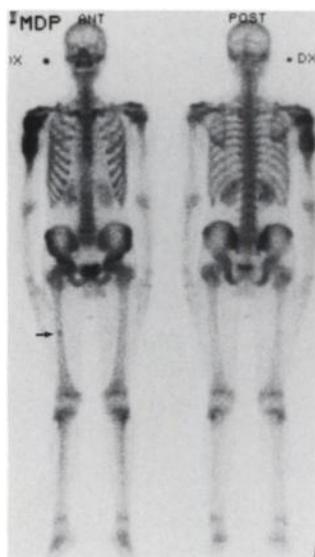


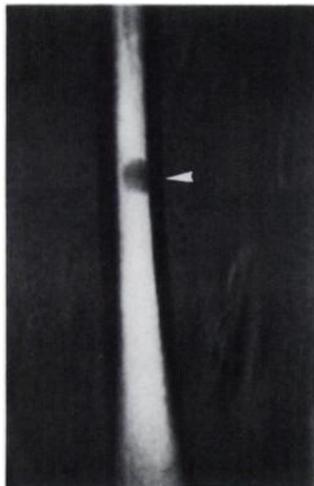
FIGURE 2. An additional area of radiotracer uptake is seen in the mid-diaphyseal area of the right femur (arrow).

femur at the site of the lesion. MRI confirmed the presence of a fairly well circumscribed intramedullary lesion (Fig. 3). Open biopsy and subsequent curettage were performed.

Six months later, MRI was performed over the area of increased tracer accumulation medially in the right pubic bone, with

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FIGURE 3. MRI examination shows a well circumscribed intramedullary lesion at the site of increased tracer accumulation in the right femur (arrowhead) (T1-weighted spin-echo sequence, coronal projection).



evidence of a well-circumscribed lesion in the medullary cavity here. An open biopsy of this lesion was also performed.

During histologic examination of the resected primary tumor, an osteoblastic osteosarcoma was found with a good response to chemotherapy [Grade III on a four-grade scale according to Rosen et al. (7)]. Biopsy specimens from the right femur and the right pubic bone showed similar patterns with no remaining viable tumor cells. New bone formation with a cellular mature osteoid tissue with focal hyalinization and calcification was observed (Fig. 4). The histopathological diagnosis in both biopsies was metastatic osteosarcoma with chemotherapy response Grade IV (7).

The finding of a devitalized metastasis in the right femur prompted additional cytostatic therapy for 4 mo, whereas the same finding in the right pubic bone resulted in no further treatment. One and a half years after the last biopsy, the patient is doing well and in the first cycle of complete remission.

DISCUSSION

Different kinds of flare responses in tumors are described in the literature. Cech et al. defines the metabolic manifestations of rapid death of neoplastic cells induced by cytostatic treatment as flare (8). Crim defines a reactive



FIGURE 4. A nonviable metastasis of osteosarcoma in the right femur (van Gieson $\times 100$).

inflammatory infiltrate adjacent to a primary neoplastic process as flare (9). For most authors, however, the flare phenomenon is synonymous with transient increased radioisotope accumulation in bone tumors after the start of systemic therapy, despite other evidences of therapeutic success (1-3, 10-11). Therapeutic success has been evaluated by either clinical or laboratory parameters or by a combination of both (1-3, 10, 11). There is no agreement on the incidence of the phenomenon or on the limitations it will have on the usefulness of radionuclide bone imaging (1, 2, 11). The appearance of new lesions as part of the flare response is considered unusual (12-14).

The reported incidence of skeletal metastases in osteosarcoma is 15%-30% (15). Early detection of these significantly affect therapy and prognosis. Whole-body bone scanning, which provides an overview of the entire skeleton, at 2-6 mo intervals has evolved as a practical clinical tool in the follow-up of patients.

Bone-seeking tracers are known to accumulate in tumors with clinical symptoms in which periosteal or cortical bone involvement can be anticipated. Little is known, however, about radioisotope accumulation in small metastatic foci, solely located in the medullary cavity. In our patient, a small, completely necrotic metastasis was found in the medullary cavity of the right femur 2 mo after normal bone scanning of the area. The scans were obtained at the beginning and end of the initial cytostatic treatment.

CONCLUSION

Our results indicate that conventional radionuclide imaging may not be as sensitive in the detection of early skeletal metastasis in osteosarcoma as commonly believed and that the flare phenomenon could account for radiotracer accumulation previously considered to represent new tumor involvement.

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