Bone Scan in Tumor-Induced Osteomalacia

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A 66-yr-old female was admitted with a 3-yr history of generalized bone pain and nasal obstruction. CT and MRI of the head revealed a large nasal mass. A whole-body bone scan revealed multifocal lesions of increased activity. Surgical removal of the nasal tumor revealed hemangiopericytoma. The patient improved clinically and a repeat bone scan 10 mo after surgery revealed markedly improved findings.

Key Words: oncogenous; osteomalacia; bone scan

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Oncogenous osteomalacia is a rarely described clinical entity that may mimic metastatic bone lesions in bone scanning. It is most commonly associated with benign tumors of mesenchymal origin and can be cured after surgical removal of the tumor. We describe a case of hemangiopericytoma causing this syndrome on serial bone scan findings.

CASE REPORT

A 66-yr-old female was admitted with a 3-yr history of generalized bone pain and nasal obstruction. CT and MRI of the head revealed a large right nasal mass extending into the left nasal cavity and destroying the medial wall of the right orbit. A whole-body bone scan revealed innumerous foci of increased activity involving bilateral ribs, skull, spine and hip joints (Fig. 1). A serum total protein, albumin, calcium and parathormone levels were normal. Alkaline phosphatase was elevated (223 U/liter: nl 30–115), while phosphorous (1.8 mg/dl: nl 2.5–4.5), 1,25 dihydroxyvitamin D (<5 pg: nl 12–40) and 25-hydroxyvitamin D (9.9 ng/ml: nl 16.0–74.0) were low. A bone marrow biopsy was negative. A biopsy of the nasal mass revealed giant cell granuloma and necrotic tissue. The nasal tumor was surgically removed and the tissue diagnosis including electron microscopy revealed hemangiopericytoma. Only focal osteoclast-like giant cells were seen. A CT 3 wk later showed complete removal of the nasal mass. The patient improved clinically; the bone pain and nasal obstruction disappeared dramatically, and serum levels of 1,25-dihydroxyvitamin D and 25-hydroxyvitamin D returned to normal. A repeat bone scan (not shown) 4 mo later still showed multiple foci of osteoblastic lesions and diffusely increased calvarial activity. The second repeat bone scan 10 mo after surgery revealed markedly improved focal lesions while diffusely increased activity, especially in the skull remained (Fig. 2).

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DISCUSSION

Tumor-induced osteomalacia or oncogenic osteomalacia is a rare phenomenon with less than 100 reported cases in the literature. Most of the tumors are benign, mesenchymal in origin and highly vascular (*1,2*). Benign tumors associated with osteomalacia include giant-cell granuloma, cavernous hemangioma, nonossifying fibroma, benign ossifying mesenchymal tumors, fibrous xanthoma, hemangiopericytoma, angiosarcoma, osteoblastoma and fibroangioma. Malignant tumors associated with oncogenic osteomalacia are extremely rare with less than 10 reported cases (*3*). There is one reported case each of prostate cancer (*4*) and oat-cell lung cancer (*5*). More common are the malignant soft-tissue sarcomas and malignant neurinoma.

The biochemical hallmark of oncogenic osteomalacia is low 1,25 dihydroxyvitamin D despite the presence of hypophosphatemia, which usually increases 1,25 dihydroxyvitamin D levels by stimulating 1α hydroxylase. The exact method by which the tumor induces these biochemical changes is not known. The most popular theory is that the tumor secretes a substance that interferes with the renal transport of phosphate and inhibits the activity of 1α hydroxylase. Miyauchi et al. (*6*) were able to induce hypophosphatemia by transplanting the tumor into athymic nude mice. In addition, extracts of the tumor inhibited 1α hydroxylase activity in cultured mouse kidney cells. More recently, Cai et al. (*7*) showed that cell culture medium containing the tumor inhibited phosphate transport in kidney cells. This inhibitory effect was lost when the medium was boiled. They argued against the factor being PTH itself since a PTH antagonist had no effect on the changes in phosphate transport; or PTH-related substances since the inhibitory effect on phosphate transport was independent of the accumulation of cAMP. This is consistent with the absence of hypercalcemia and elevated PTH in patients with oncogenic osteomalacia.

Once the tumor is discovered, surgical resection should be attempted. Resection of the tumor, especially if it is benign, can lead to permanent cure of the osteomalacia (*1,8,9*). Even partial resection of the tumor can result in amelioration of the symptoms (*8*). Malignant tumors are more resistant to surgical resection, especially if metastases have occurred (*3*). Medical treatment with vitamin D

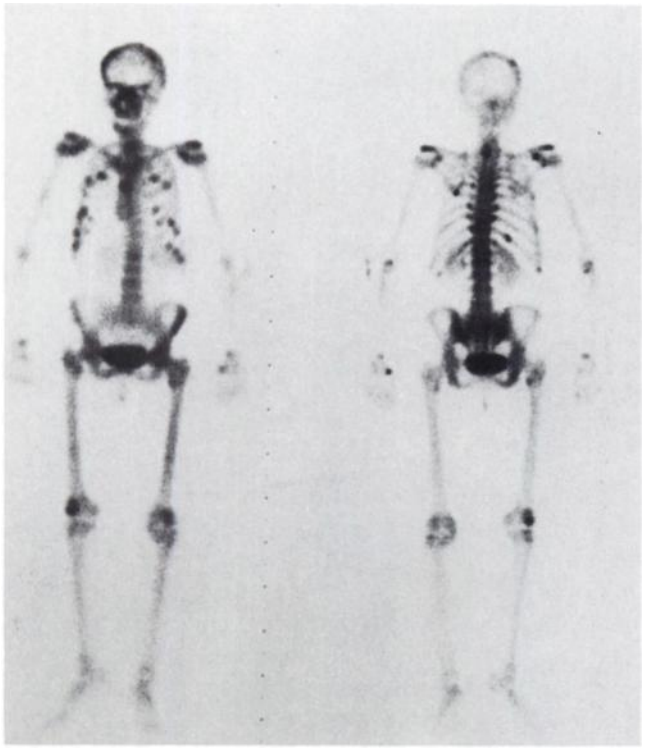

FIGURE 1. Initial whole-body bone scan shows multifocal osteoblastic lesions involving bilateral ribs, skull, spine and hip joints.

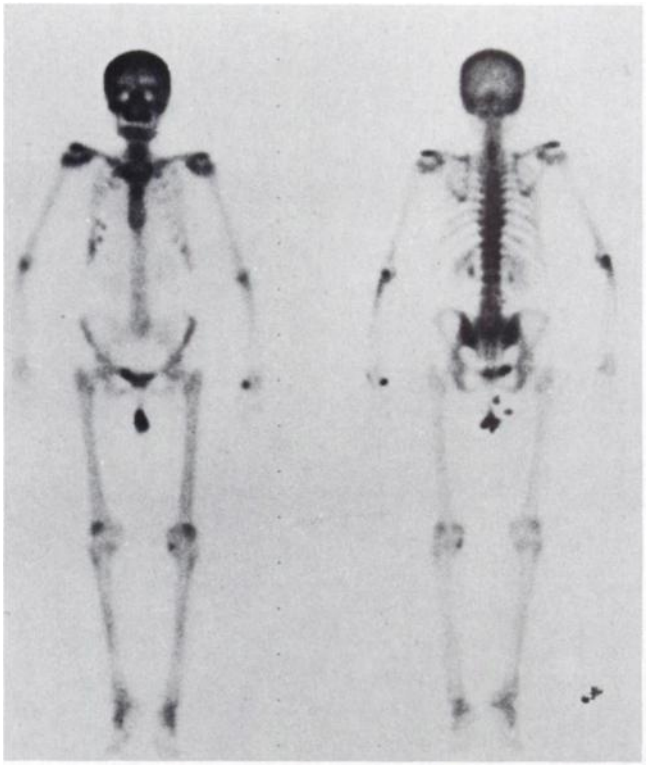

FIGURE 2. Repeat scan 10 mo after surgery shows largely disappeared focal lesions.

and oral phosphate supplements has a variable response (*1*).

The bone scan pattern in typical (nontumor-induced) osteomalacia can be focal, similar to osseous metastases, or diffuse (*10–13*). There are very few descriptions of bone scan findings in oncogenous osteomalacia, and none in the nuclear medicine literature. Two case reports of oncogenic osteomalacia, in which bone scan results are mentioned, sited multiple foci of increased radiotracer uptake on the bone scans (*14,15*) as in our case; and there is one report of generalized increased radiotracer uptake on the bone scan (*1*). The pattern of uptake in oncogenic osteomalacia and osteomalacia secondary to other causes (e.g., malabsorption, renal failure, vitamin D deficiency, drugs, etc.) is probably indistinguishable.

This case illustrates that though the patient is known to have a tumor, the behavior of the tumor cannot be implied when the bone scan reveals a pattern that is highly consistent with diffuse osseous metastases. Without knowing the malignant nature of the tumor, the presence of multiple, randomly placed abnormal radionuclide accumulation does not necessarily equate with the presence of osseous metastases. The interpretation of osseous metastases should be read with caution; only if the tumor is known to be malignant and there are no metabolic causes that would explain the findings. Perusal through the laboratory data is helpful to eliminate metabolic causes, specifically looking at calcium, phosphate, creatinine, PTH and 1,25-dihydroxyvitamin D levels. A bone biopsy may be necessary to diagnose osteomalacia, especially if the tumor has not been identified. Interestingly, in this case, after surgical resection of the tumor, the patient's symptoms improved dramatically and the focal abnormalities seen on the initial bone scan resolved on the follow-up scan 10 mo later. This correlates well with the clinical experience reported in the literature.

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FIRST IMPRESSIONS

Extensive Bone Infarction Secondary to Perifemoral Abscess

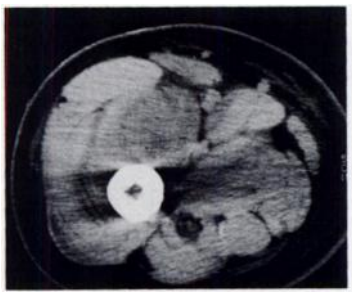

FIGURE 1.

FIGURE 2.

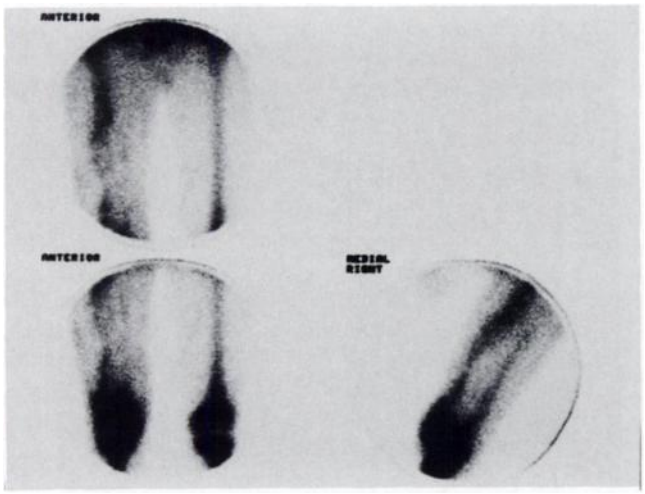

FIGURE 3.

PURPOSE

A 14-yr-old male who presented with fever and confusion 3 days after a minor, closed injury to the right thigh. S. aureus septicemia was detected. He subsequently developed progressive swelling of the right thigh. Computed tomography (Fig. 1) showed edema in the right vastus compartment. Surgical drainage revealed an abscess surrounding the right femur. The periosteum was absent from the exposed bone. Muscle biopsy demonstrated infectious myositis. Bone biopsy demonstrated osteomyelitis and necrosis. S. aureus was cultivated from femoral marrow. A bone scan (Fig. 2) showed absent uptake in the mid/lower right femoral shaft. A gallium scan (Fig. 3) showed a rim of increased uptake in the thigh and absent uptake in bone. The final diagnosis was infarction of the right femur secondary to perifemoral abscess and osteomyelitis. There was no evidence of hemoglobinopathy. The proposed mechanism was thrombotic occlusion of nutrient arteries and local destruction of the periosteum.

TRACER

Technetium-99m-MDP (700 MBq)

ROUTE OF ADMINISTRATION

Intravenous injection

TIME AFTER INJECTION

Three hours

INSTRUMENTATION

Gamma camera

CONTRIBUTORS

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