"COLD" LESIONS ON BONE IMAGING

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Photon-deficient foci or "cold" lesions were demonstrated on ^{99m}Tc-polyphosphate bone imaging in eight individuals with various malignancies and one in sickle cell crisis. The bone radiographs of five of these persons failed to show corresponding bony changes at the time of the imaging. Most of the "cold" lesions observed on bone imaging were located in the denser and tubular bones.

A postulate has been advanced regarding the factors that might influence the different gamma-imaging manifestations of radiographically demonstrable lytic lesions.

The cases presented herein further emphasize the importance of recognizing the existence of "cold" areas in the images of bones and the need to place these in proper perspective when interpreting scans.

In gamma images of bone, increased activity that may be localized or widespread, symmetric or nonsymmetric, is the usual manifestation of malignant or nonmalignant skeletal disease. Nevertheless, there have been isolated reports of "normal" bone images in patients with proven malignant bone involvement (*1–6*). Recently, Goergen, et al (*7*) described seven instances of photon-deficient ("cold") lesions in patients with bone disease. In this communication we present eight patients with malignant bone disease and one with sickle cell anemia who demonstrated "cold" lesions on ^{99m}Tc-polyphosphate bone imaging.

PATIENTS AND METHODS

Pertinent clinical and laboratory data for each patient are summarized in Table 1. Patients received 15 mCi of ^{99m}Tc-polyphosphate intravenously; approximately 3 hr later imaging was performed with a Model 84 5-in. dual-probe Ohio-Nuclear scanner adapted with a 3-in. focal depth, low-energy collimator. Minified 1:5, total-body images were obtained using a scan speed adjusted to obtain an information density of about 450 counts/cm^2. Regions of interest such as vertebrae, rib cage, pelvis, and hands were routinely imaged using an upgraded 2-C Picker Dynacamera equipped with an ultrafine collimator.

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TABLE 1. PERTINENT CLINICAL AND LABORATORY DATA

Patient	Age/Sex	Calcium (mg%)	Phosphorus (mg%)	Alkaline phosphatase IU	Diagnosis
1	60/M	7.6	2.7	48	Metastatic carcinoma; unknown primary
2	29/M	8.7	4.9	110	Sickle cell crisis
3	61/F	8.3	2.9	1300	Metastatic carcinoma; unknown primary
4	51/F	8.4	2.7	250	Breast carcinoma
5	65/M	9.5	3.0	67	Lung carcinoma
6	51/F	10.6	3.6	132	Breast carcinoma
7	51/F	9.2	2.8	99	Lung carcinoma
8	76/M	10.3	3.6	311	Breast carcinoma
9	83/M	8.3	2.5	190	Transitional-cell carcinoma; urinary bladder

TABLE 2. COMPARISON OF IMAGING AND RADIOGRAPHIC RESULTS

Patient	Imaging	Radiograph*
1	Multiple "cold" lesions of the spine; D_3, D_7, D_{12}, and L_3	Negative
2	"Cold" lesions in the tarsals of each foot	Negative
3	"Cold" lesion, right lateral aspect of D_8	Negative
4	"Cold" areas in L_5 and left lateral aspect of sacrum	Destroyed pedicles D_5 and L_5; lytic metastases in pelvis
5	"Cold" lesion, 12th rib, posteriorly	Negative
6	"Cold" areas, D_3, D_4, D_5, D_9, and D_{11}. D_9–D_{12}, left lateral aspect, and L_1, show "hot" activity	Diffuse lytic metastases, dorsal and lumbar vertebrae
7	Multiple "cold" foci, interspersed with "hot" lesions—spine	Negative
8	"Cold" activity in L_4, L_5, and D_{12} is equivocal	Osteoblastic metastases in lumbosacral vertebrae
9	"Cold" areas—L_1, L_2, and L_3	Suspicious lytic lesions of dorsal and lumbar vertebrae

* Radiographic interpretations limited to abnormal areas seen on imaging.
"Lytic" refers to lesions with well-circumscribed borders and "cold" refers to those without.

A preset time of 3 min was used in obtaining each view. When clinically indicated, the skull and other appendicular bones were also included in the camera imaging.

Patient 1 also had a bone marrow radionuclide study obtained 48 hr after the intravenous administration of 3 mCi of ^{111}In-chloride.

Abnormal imaging findings were compared with radiographs of corresponding regions whenever available.

RESULTS

Table 2 is a summary of the localization of "cold" lesions on imaging and the corresponding radiographic findings for the same areas. The "cold" lesions on Patients 1, 2, 3, 5, and 7 showed no corresponding abnormal findings on radiographs.

DISCUSSION

The occurrence of "cold" lytic-like or photon-deficient lesions in bone imaging is probably uncommon; we encountered only nine instances among more than 300 bone scans performed at our institution. It should be pointed out, however, that aside from the regular minified scans, photoscans obtained were limited routinely to the spine, rib cage, pelvis, and hands; occasionally, when clinically indicated, the skull and other bones were included.

In our experience and that of others, lytic lesions seen on radiographs may manifest as areas of increased ("hot") (*8,9*), normal (*2,7*), or decreased ("cold") (*7,10*) activity on bone scanning. We postulate that the type of imaging recorded from a radiographically evident lytic lesion largely depends on the size of the lytic area and the degree of reactive bone process and its vascularity (Fig. 1). Thus, for example, a lytic area 2 cm in diameter with sufficient reactive bone tissue and vascularity might appear as a "hot" lesion. On the other hand, a focus, regardless of size, that has limited reactive bone tissue and vascularity, sufficient to compensate only for the photon-deficient lytic area, may not become evident, appearing as a normal area. A lytic lesion larger than 2 cm but possessing relatively less reactive tissue vascularity around it (thus insufficient to obscure the photon-deficient area) may manifest as a "cold" or lytic area on imaging.

The preceding postulate takes into consideration only "cold" lesions showing corresponding lytic changes on radiographs. There are, however, times when the "cold" lesions appreciable on bone imaging are not disclosed as lytic findings on concurrent radiographs. Goergen, et al described two such examples, and Patients 1, 2, 3, 5, and 7 in our series also illustrate such a category. As noted by these investigators, this imaging observation may be related to a direct interruption of perfusion to a particular osseous region, whether this be caused by trauma,

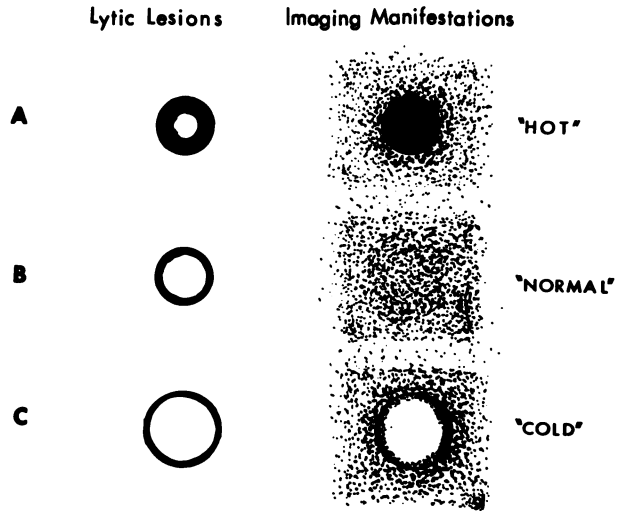

FIG. 1. Schema of possible manifestations of lytic foci on imaging. (A) Two-centimeter lesion with very active reactive tissue and vascularity; (B) 2-cm lesion with limited reactive tissue and vascularity, but sufficient to obscure lytic focus; and (C) lesion over 2 cm with limited reactive tissue and vascularity, but sufficient to outline border of lysis.

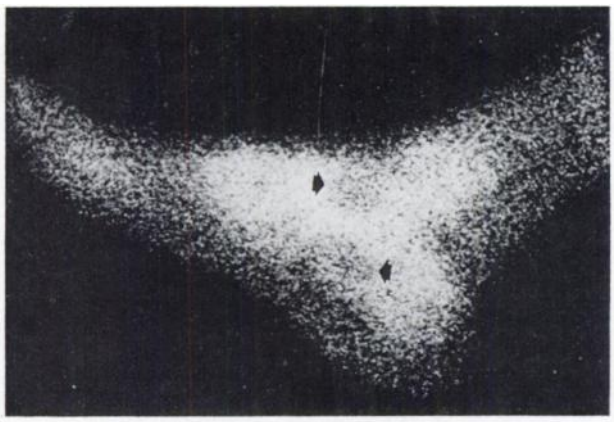

FIG. 2. "Cold" lytic areas (arrows) in tarsals of sickle cell patient in crisis (Patient 2).

infarction, or sludging of cells in the blood vessels. The "cold" lytic lesions in both ankles of Patient 2 are most probably due to infarction since in this patient with sickle cell anemia severe bone pain was experienced in each foot at the time of the study (Fig. 2). Patient 1 showed an anaplastic cell-packed marrow of undetermined origin on bone biopsy. Bone marrow imaging using ^{111}In-chloride in this patient also demonstrated, but with poorer resolution, the photon-deficient areas manifested on bone imaging (Fig. 3A and B). The absence of any evident change on radiographs such as lysis or sclerosis in these five patients may possibly indicate a relatively more acute or recent bone involvement (Fig. 3C). It is interesting that three of these patients (1, 2, and 5) have the lowest levels of alkaline phosphatase. However, Patient 3 had the highest alkaline phosphatase as a result of widespread hepatic metastases verified at surgery.

It is noteworthy that six of the patients described by Goergen, et al manifested "cold" or photon-deficient lesions primarily of the vertebrae or ends of long bones. Likewise, eight of our nine patients, showed involvement localized to the denser and tubular bones. We believe the "cold" lesions involving the vertebrae and the ends of long bones are easier to discern than are lesions elsewhere because they are invariably adjacent to intact bone that would normally possess a relatively higher radiopharmaceutical uptake. An exception is Patient 6, who demonstrated on photoscan a "cold" lesion in the 12th rib posteriorly on the right. This "cold" lytic area was not resolved as such on the regular minified scan; instead, it appeared as an area of increased activity. The detection of these photon-deficient lesions may be enhanced when they occur in abnormal bony tissue with increased activity, as observed in metastatic disease. Examples of the latter may be found in Patients 5, 6, 7, and 8 (Fig. 4).

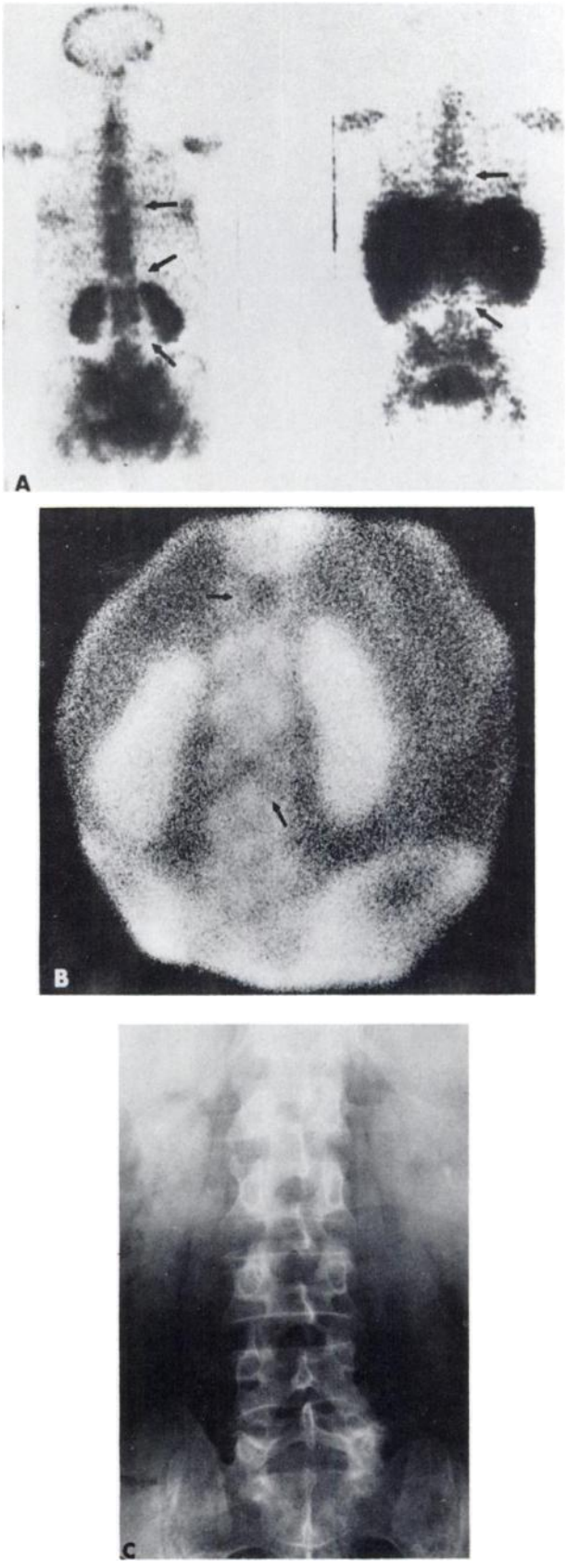

FIG. 3. (A) Photon-deficient foci (arrows) in spine, on bone and bone marrow images (Patient 1). (B) Photoscan closeup of spine image in same patient (Patient 1). (C) Negative radiograph of lumbar spine (Patient 1).

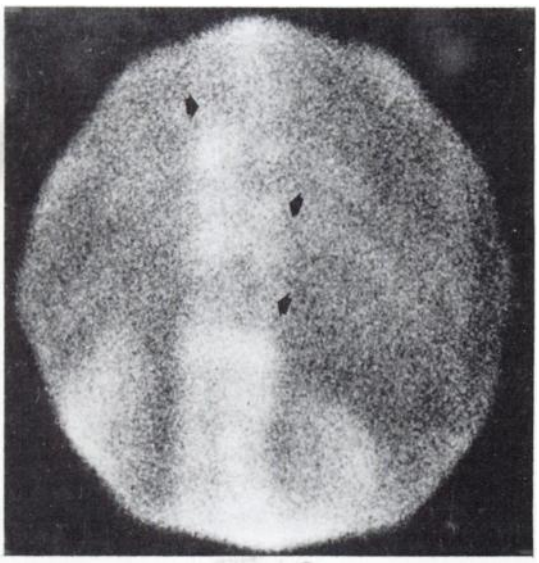

FIG. 4. Photon-deficient lesions (arrows) are seen better when located adjacent to "hot" areas (Patient 7).

Donnelly and Johnson (*8*) reported a patient with lung carcinoma who demonstrated lysis of the clavicle on radiography, but "hot" activity on imaging. Similarly, Pendergrass and associates (*10*) described a patient with a lytic area in a carpal bone that manifested increased activity on imaging. Thrall's group (*9*) reported, on the other hand, a large lytic lesion with a well-circumscribed rim of activity involving a great portion of the frontoparietal bones of one side.

We concur with Goergen and associates that a reassessment of bone-imaging interpretation is in order in view of the recognition of the existence of photon-deficient ("cold") foci. The cases described here further emphasize such a need particularly in those instances in which other conventional methods of evaluating bone disease have failed to show involvement.

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