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The Role of Whole Body Bone Scan in Bronchogenic Carcinoma

Kiho Kim, Kyung Rae Kim, Hee Young Sohn, Uk Yong Lee, Sung Kyu Kim, Won Young Lee

Department of Internal Medicine Yonsei University, College of Medicine, Seoul, Korea

One hundred and sixty patients having bronchogenic carcinoma were evaluated for bone metastasis by means of 99mTc-monodiphosphate bone scanning, correlative radiographic bone survey and their clinical findings. In all patients, diagnosis was histologically proved. Bone scan demonstrated the possible evidence of bone metastasis in 75 patients (46.9%) and radiography, in 29 patients (18.1%). False negative was noted in 1 patient. Bone scan correlated with radiography in 37.3%, and with accompanying bone pain in 52% of the patients. But there was no correlation with the level of serum calcium, inorganic phosphorus and alkaline phosphatase. In connection with their clinical stages before scanning, bone scans were positive in 33.3% of clinical stage I, 10.8% of clinical stage II and 54.1% of clinical stage III. Our study suggests that bone scanning with 99m-monodiphosphate detected early bone metastasis in patients with bronchogenic carcinoma before their lesions became evident clinically or radiographically, and also important to determine operability.

Key Words: Whole Body Bone Scan, Bronchogenic Carcinoma.

Cancer of the lung continues to be a diagnostic and therapeutic challenge to the chest physician and thoracic surgeons despite sophisticated investigative procedures, refined surgical techniques, and improved radiotheraphy. Frequently, cancer has spread beyond the confines of the therapeutic field at the time of diagnosis. Numerous reports insist that more than half the cases have distant metastasis including skeletal involvement. Therefore early identification of latent bone metastasis is of value in the management of patients with lung cancer. Whole body skeletal imaging with Technetium 99m-monodiphosphate is now widely accepted as an excellent technique to search for bone metastasis in patients with malignant neoplasm though the accumulation does not always correspond directly to the metastasis. This paper reports our clinical experience with 160 consecutive patients with lung cancer. The patients were prospectively evaluated for bone metastasis by means of radioisotope scanning using technetium 99m-monodiphosphate and correlative bone radiography.

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MATERIAL AND METHODS

One hundred and sixty cases of bronchogenic carcinoma evaluated at Severance Hospital were reviewed. Radioisotope bone scan and radiographic bone survey were done in addition to the conventional diagnostic lung cancer workup. Bone scan was performed by intravenous administration of 99mTc-monodiphosphate in a dose of 20 mCi. Whole body bone scan images were made after four hours on the gamma camera (CGR-Opticamera).

RESULTS

Our cases consist of 126 males and 34 females showing a male to female ratio of 3.7:1. The mean ages were 58.7 and 57.9 respectively with the peak incidences in the 6th and 7th decades (Table 1). Histological diagnosis in 81 patients (50.6%) was epidermoid carcinoma, 27 (16.9%) with small cell unidifferentiated carcinoma, 27 (16.9%) with adenocarcinoma, 21 (13.1%) with large cell undifferentiated carcinoma, and 4 (2.5%) with unclassified types (Table 2). The diagnosis of lung cancer in all patients was histologically proved using the procedures shown in (Table 3). In 85 cases, cell diagnosis was obtained by bronchoscopic biopsy, 38 cases, by peripheral lymph node biopsy, 15 cases, by sputum cytology only, 8 cases, pleural biopsy, 6 cases, bone biopsy, 2 cases mediastinal lymph node biopsy, 2 cases, percutaneous needle lung biopsy, 2 cases, thoracotomy with biopsy, 1

Table 1. Age and sex distribution

Age	Male	Female	Total
0 – 10	–	–	–
11 – 20	–	–	–
21 – 30	2	1	3
31 – 40	2	2	4
41 – 50	16	7	23
51 – 60	44	13	57
61 – 70	51	8	59
71 – 80	11	3	14
Total	126	34	160

M:F = 3.7:1

Table 2. Cell types of lung cancer

Cell type	No. of cases	%
Epidermoid Ca.	81	50.6
Small cell undifferentiated Ca.	27	16.9
Adenocarcinoma	27	16.9
Large cell undifferentiatedCa.	21	13.1
Unclassified	4	2.5
Total	160	100.0

Table 3. Methods of obtaining tissue diagnosis

Procedure	No. of cases
Bronchoscopy with biopsy	85
Lymph node biopsy	38
Sputum cytology only	15
Pleural biopsy	8
Bone biopsy	6
Mediastinal biopsy	2
Percutaneous lung biopsy	2
Thoractomy with biopsy	2
Lobectomy	1
Chest wall mass biopsy	1
Total	160

Table 4. Results of bone scan and X-ray survey

Result	Bone Scan	X-ray survey	
		Positive (%)	Negative (%)
Positive	75	28(37.3)	47(62.7)
Single	34	12(35.3)	22(64.7)
Multiple	41	16(39.0)	25(61.0)
Negative	85	1(1.2)	84(98.8)
Total	160	29(18.1)	131(81.9)

Table 5. Comparison of bone scan and X-ray survey and other clinical findings

Bone scan	X-ray survey	Bone pain	Ca	P	Alk. P
Positive	*Positive*	*Positive*	0/21	2/21	10/21
Positive	*Positive*	Negative	0/7	1/7	4/7
Positive	Negative	Positive	1/18	1/18	8/18
Positive	Negative	Negative	1/29	1/29	13/29
Negative	*Positive*	Negative	0/1	0/1	0/1
Negative	Negative	*Positive*	2/13	2/13	4/13
Negative	Negative	Negative	2/71	4/71	22/71

Ca: above 10.5mg/100ml
P: above 4.5mg/100ml
Alk. phosphatase: above 115.0mg/100ml

case, lobectomy and 1 case, chest wall mass biopsy. With a bone scan, 75 patients (46.9%) had positive results suggesting metastasis; 85 (53.1%) had negative results. With a bone radiograph, 29 patients (18.1%) had a positive result; 131 (81.9%), had a negative result. In 75 bone scan positive patients, radiographic survey revealed a positive results in 28 cases (37.3%) and in 47 (62.7%), a negative result. In 34 cases which showed a single hot uptake

Table 6. Incidence of hot areas on bone scan in various cell types

Cell type	No. of cases	%
Epidermoid Ca.	33/81	40.7
Small cell undifferentiated Ca.	10/27	37.0
Adenocarcinoma	15/27	55.6
Large cell undifferentiated Ca.	14/21	66.7
Unclassified	3/4	75.0
Total	75/160	46.9

Table 7. Distribution of hot areas on bone scan in 75 cases

Site	Epidermoid	Small cell	Adenoca.	Large cell	Unclassified
Skull	••	•	•	•	•
Spine					
Cervical	•••	•		••	
Thoracic	••••• •••••	•••	•••	••••	•
Lumbar	•••••	••	••••• ••	••••	•••
Ribs	••••• ••••• ••••• ••••• •	••••	••••• •••••	••••• •••••	•
Pelvis	•	•	••		
Expremity					
Upper	•••••	•	••		
Lower	••••• •••••	•	•	••	

in the bone scan, the radiographic survey disclosed positivity in 12 cases (35.3%). In 41 cases which showed multiple hot uptakes in the bone scan, the radiograph revealed positive result in 16 cases (39.0%). There was only one case (1.2%) of a negative scan and positive radiographic finding (Table 4). There appeared a poor correlation between the bone scan positivity and the level of serum calcium, inorganic phosphorus and alkaline phosphatase (Table 5). The incidence of hot areas on the bone scan according to the cell type was 40.7% in epidermoid carcinoma; 37.0%, small cell undifferentiated carcinoma; 55.6% in adenocarcinoma; 66.7%, large cell unidifferentiated carcinoma; and 75% in unclassified tumor type (Table 6). The anatomical distributions of the hot area are shown in (Table 7).

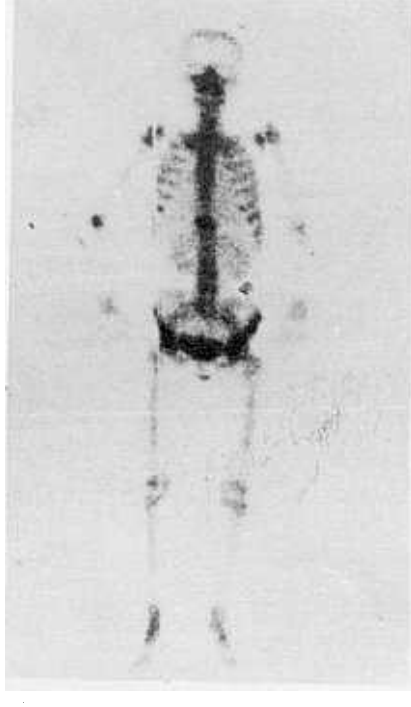
The most frequent sites of probable metastasis in all cell types was the rib, which was followed by vertebrae and the extremities. The relationship between bone scanning and clinical staging was demonstrated in (Table 8). In the clinical stage III, more than half the cases have hot area on bone scan. Typical cases of metastatic bone scan images were demonstrated in (Figure 1).

Table 8. Results of bone scan to the clinical stage

Clinical stage	Bone Scan positive cases	%
I	2/ 6	33.3
II	6/ 32	18.8
III	66/122	54.1
Total	74/160	46.3

DISCUSSION

Since the introduction of 99mTc-labeled skeletal agents, total body bone imaging has played an increasingly important role in the



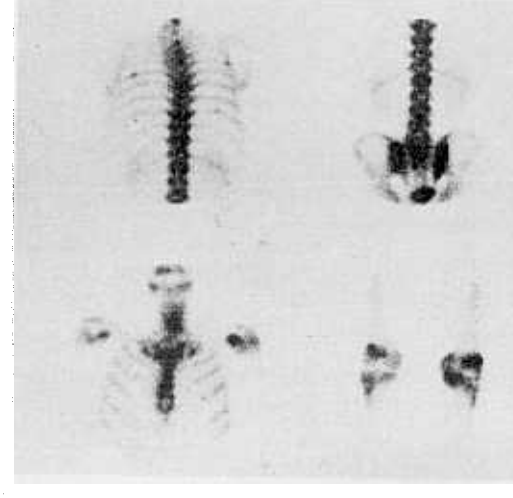


Fig. 1. A. Anterior view of whole body bone scan showing multiple leisons in the skull base, vertebral column, ribs and pelvis resulting from metastatic disease.

B. Bone scan revealing widerspread metastatic deposits in the spine sacrum, sternum, humerus and femur.

evaluation of patients with lung cancer (Antonio, et al, 1979; Belliveau and Spencer, 1975). It is a sensitive and accurate method and has been demonstrated to be superior to evaluation via blood chemistry levels or routine skeletal radiographic survey (Borak, 1942). When correlated with clinical signs and radiographs, bone scans may demonstrate metastasis in the presence of primary malignancy (Cavalieri and Scott, 1968). The radionuclide label, technetium-99m, is readily available and relatively inexpensive, its low gamma emission allows these complexes to be used with either the rectilinear scanner or stationary camera devices. Finally, use of the radiopharmaceuticals has allowed considerable cost reduction in bone scanning. At present, this agent is the choice for bone scanning techniques (Borak, 1942). It is well established that alterations in bone physiology and bone pathology will produce an abnormal bone scan. The mechanism of the image formed by radionuclide deposition helps explain its sensitivity. The radiopharmaceutical reaches the osseous structures by way of the vascular system. Processes that increase blood supply or bone blood flow increase the amount of material reaching that area (Corcoran, et al, 1976). Other repair mechanism include altered exchange processes in new bone formations, and increased turnover, all contribute to the area of increased radioisotope activity noted. On a bone scan, as a result of this relationship between bone blood flow and bone cellular kinetics, even minor alterations in the normal osseous state will produce an abnormal bone scan. Consequently osteolytic and osteloblastic leisons, as well as areas which may appear normal radiographically, will appear as positive areas on a scintiscan (Edeldtyn, et al., 1969). In our study, radioisotope scans, were 46.9% of the cases and correlation with radiographic survey was 37.3%, and with accompanying bone pain, 52%. Bone scans detected metastatic leisons when bone radiographs did not in 29.4% of our patients. Pistenma and co-workers (DeNardo et al., 1967) reported that 54% of their patients with lung cancer had positive bone scan but negative radiographis. The percentage of positive scans is a little lower in our series. Gutierrez and associates (Fletcher, et al., 1975) demonstrated that bone scan detected osseous metastasis in 56% of their patients, as proved by post-mortem examination. They also noted that bone scans correlated with clinical, Corcoran and colleagues (Gutierz, et al, 1975) reviewed 266 patients with primary lung cancer of whom 53% with abnormal bone scan had metastatic bone involvement. An accurate correlation of bone scans and postmortem findings would require postmortem examination of all bones showing increased radioisotope uptake. However this is not performed as a routine procedure in our institute. Doubtful bone scans may be confirmed by open or needle biopsy. The incidence of bone metastasis detected by routine radiographic survey was 18.1% in our series. Similarly Donato *et al* (Caralieri and Scott, 1968 Gutierz, et al., 1975) reported 16.6% osseous metastasis at the time of initial evaluation. Bone metastasis is a well recognized frequent late manifestigation of lung cancer often identified radiographically in the advanced stage of the disease. Skeletal metastasis often becomes visible by radiographs when there is 30 to 50% bone demineralization (Gatiearz, et al., 1975) or when 50 to 75% cancellous bone destruction is present (Corcoran, et al., 1976). With accelerated mineral turnover and new bone formation, a scan can detect bone metastasis earlier than bone radiographs (Pistenma, et al., 1975). Not infrequently, destructive leisons in the vertebrae must be greater than 1.5cm in size to be seen (Hiyoshimau et al., 1978). It is

well documented that scintiscanning techniques frequently will demonstrate skeletal metastasis before they may be appreciated on radiographs. In addition, scanning techniques yield a much lower false-negative rate than roentgenograms. O'Mara (Borka, 1942) suggested that the appearance of a leison on a scintiscan will predate radiographic visualization by 3 to 6 months. Furthermore, in patients with positive roentgenogram, the scan will not infrequently show that the amount of metastatic disease present is far greater than considered radio-graphically (Hiyoshimaru, et al., 1978). Scanning techniques will allow for optimization of sites for biopsy purposes. Scans are also extremly useful in evaluating areas such as the sternum and scapulae that are difficult to study by radiographic techniques (Borak, 1942; DeNardo, et al., 1967). Scanning techniques do contain a small percentage (3 to 8%) of false-negatives. These usually occur in patients with highly anaplastic tumors or in patients with slowly growing indolent leisons where reactive bone does not form or is not detectable (Borka, 1942; Edeldtyn, et al., 1967). The problems of false-positive scan was encountered in all anatomic sites. The highest percentage occured in the ribs and costochondral junction, where prior episodes of trauma may have been forgotten by patients. A wide variety of normal variants and benign diseases will result in positive bone scans. Such benign processes that may result in positive scan findings include arthritides, fractures, osteomyelitis, previous surgery regional migratory osteoporosis, as well as normal varients (Borka, 1942; Gutierz, et al., 1975). Corcoran and colleagues (Gutierrz, et al., 1975) introduced the following guidelines to be useful in interpreting equivocal scan abnormalities. (a) Radiographic examination must be obtained of the areas corresponding to all solitary scan abnormalities. (b) Physical examination is extremely important. Unexplained skeletal pain and tenderness in the cancer patients may be due to metastasis. (c) By anatomic region, the lowest percentage of confirmed metastasis was in the ribs; solitary abnormalities in them must be regarded with particular suspicion; (d) Biopsy should be considered in patients with a normal radiograph and an abnormal scan (Gutierrz, et al., 1975; Robert, 1976). (e) In addition to metastasis, the differential diagnosis for solitary scan abnormalities includes degenerative arthritis, trauma, primary benign bone lesions, and apparently idiopathic cases for which no explanation can be found. Attempts at using secondary scanning agents to increase the specificity of bone imaging have not been totally succesful. So-called "tumor-scanning agents" such as gallium-67 citrate and indium-111 bleomycin have proven to be of little value in this effort (13). Some promise is offered by the use of sodium selenite labeled with selenium-75 in allowing differentiation between malignant and benign osseous disease (14). However, the nonspecificity of routine bone scanning today remains a problem to be solved.

CONCLUSION

Although often nonspecific, bone scanning techniques remain a sensitive and accurate method for detection of bone metastasis of bronchogenic carcinoma. Our study has shown that bone scanning is a more sensitive and reliable tool than bone radiography in the evaluation of patients with lung cancer. Scans detected early bone metastasis before the lesions became evident clinically and radiographically. That technetium 99m-monodiphosphate scanning is easy to use, is widely available, and is nontoxic with low radiation, should make this procedure valuable during the evaluation of patients with lung cancer for management.

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