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Ectopic accumulation of ^{99m}Tc-HMDP in primary lung cancer in comparison with CT findings

Shoji YOSHIDA,* Mitsutaka FUKUMOTO,* Naoko YOSHIMURA,*
Kayoko OOBAYASHI** and Yoshiki TAKADA**

** Department of Radiology, Kochi Medical School*
*** Department of Radiology, Hyogo Medical Center for Adults*

The purpose of this study was to evaluate the frequency and the extent of extraosseous ^{99m}Tc-HMDP accumulation in 412 patients with primary lung cancer.

CT scanning was also performed and we compared the extraosseous uptake by lung cancer with the internal structure of the tumor on CT scans. The extent of ectopic ^{99m}Tc-HMDP accumulation was classified as low, moderate or high. CT scans were used to evaluate the size and internal structure of the tumor, including calcification and necrosis.

Ectopic ^{99m}Tc-HMDP accumulation in primary lung cancer was found in 32 patients (7.7%), and included 2 cases (0.5%) of high uptake, 8 cases (1.9%) of moderate uptake, and 22 cases (5%) of low uptake. No difference in uptake was observed among the histological types, but a relationship between tumor size and ^{99m}Tc-HMDP extraosseous accumulation was observed. CT scans of the 32 tumors exhibiting ectopic ^{99m}Tc-HMDP accumulation revealed 5 cases of calcification in the tumor and 18 cases of tumor necrosis. The factors promoting ectopic ^{99m}Tc-HMDP accumulation were considered to be tumor size and calcification or necrotic change. In patients with neither calcification nor necrosis, other factors such as increased calcium metabolism and altered vascular permeability may be involved.

Key words: ectopic accumulation of ^{99m}Tc-HMDP, primary lung cancer, CT findings

INTRODUCTION

ACCUMULATION of bone scanning agents in primary lung cancers has already been the subject of a few case reports,[1-3] but the factors responsible for this phenomenon have not been clearly demonstrated. In this study, we evaluated the frequency and the extent of ^{99m}Tc-HMDP accumulation in 412 patients with primary lung cancer. To investigate this ectopic accumulation, CT scanning was also performed close to the time of bone scanning.

MATERIALS AND METHODS

A total of 412 patients with primary lung cancer were examined, including 123 with squamous cell carcinoma, 182 with adenocarcinoma, 62 with small cell carcinoma, 15 with large cell carcinoma and 30 with histologically undefined cancer.

Bone scans were obtained simultaneously in the anterior and posterior projections by means of a whole body scinticamera (GCA-90A-E2) with a low-energy high-resolution collimator. Scanning was performed 3 hours after intravenous injection of ^{99m}Tc-HMDP at a dose of 740 MBq. The extent of ectopic ^{99m}Tc-HMDP accumulation was classified as follows: low uptake (+) (less than the physiological rib uptake), moderate uptake (++) (equal to physiological rib uptake), and high uptake (+++) (higher than physiological rib uptake).

CT scans (TCT-900S) were obtained to evaluate the size and internal structure of the tumor, including the presence of calcification and necrosis.

RESULTS

Thirty-two patients showed signs of ectopic ^{99m}Tc-HMDP accumulation in their primary lung cancer, corresponding to 7.7% of all examined cases. They included 2 cases

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For reprint contact: Shoji Yoshida, M.D., Department of Radiology, Kochi Medical School, Kohasu, Okoh-cho, Nankoku, Kochi 783, JAPAN.

Table 1 The summary of the findings for ^{99m}Tc-HMDP accumulation cases

Case	Histology	Tumor size (cm)	Degree of Abn. accum.	Calcification	Necrosis
1) I.H.	SCC	8 × 12	High (+++)	+	+
2) E.H.	SCC	10 × 8	High (+++)	+	-
3) T.T.	SCC	7 × 7	Moderate (++)	−	+
4) M.K.	Adeno	3.5 × 3.5	Moderate (++)	−	-
5) T.T.	SCLC	5 × 5	Moderate (++)	−	+
6) M.H.	SCC	8 × 7	Moderate (++)	+	-
7) T.N.	Adeno	5 × 9	Moderate (++)	−	-
8) E.T.	SCC	8 × 5	Moderate (++)	−	-
9) S.Y.	SCLC	7 × 7	Moderate (++)	−	+
10) M.T.	Adeno	9 × 10	Moderate (++)	+	-
11) T.K.	SCC	6 × 6	Slight (+)	−	+
12) A.K.	SCLC	8 × 8	Slight (+)	−	+
13) S.H.	SCLC	8 × 5	Slight (+)	−	+
14) T.I.	SCLC	6 × 7	Slight (+)	−	+
15) T.K.	Adeno	2.5 × 2.5	Slight (+)	−	+
16) S. S.	SCLC	7 × 5	Slight (+)	−	+
17) K.K.	Adeno	4 × 4	Slight (+)	−	-
18) S.K.	Large	4 × 4	Slight (+)	−	+
19) T.S.	Large	3 × 3	Slight (+)	−	-
20) M.A.	SCLC	4 × 4	Slight (+)	−	+
21) Y.Y.	Adeno	6 × 6	Slight (+)	−	+
22) M.T.	SCLC	6 × 7	Slight (+)	−	+
23) K.I.	Adeno	8 × 10	Slight (+)	−	+
24) G.T.	SCC	4 × 5	Slight (+)	−	+
25) M.I.	Adeno	7 × 6.5	Slight (+)	−	−
26) K.K.	Adeno	10 × 5	Slight (+)	−	−
27) T.Y.	SCC	5.5 × 6.5	Slight (+)	−	+
28) I.T.	Adeno	2.5 × 2.2	Slight (+)	−	−
29) Y.U.	SCC	5 × 5	Slight (+)	+	−
30) T.H.	SCC	4.2 × 5.2	Slight (+)	−	−
31) S.F.	Adeno	6 × 6	Slight (+)	−	−
32) K.T.	SCC	7 × 7	Slight (+)	−	+

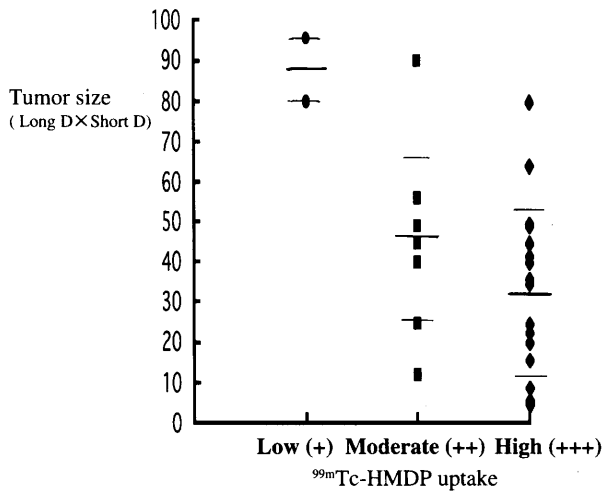

Fig. 1 Relationship between ^{99m}Tc-HMDP uptake and tumor size.

(0.5%) of high uptake, 8 cases (1.9%) of moderate uptake and 22 cases (5.3%) of low uptake. The histological diagnosis was as follows: 11 SCCs (34%), 11 adenocarcinomas (21%), 8 small cell carcinomas (21%) and 2 large cell carcinomas (6%).

While the 2 patients with high uptake had SCC, the 8 patients with moderate uptake had SCC (n = 3), adenocarcinoma (n = 3), and small cell carcinoma (n = 2). In addition, the 22 patients with low uptake had SCC (n = 6), adenocarcinoma (n = 8), small cell carcinoma (n = 6) and large cell carcinoma (n = 2). CT scans of these 32 cancers with ectopic ^{99m}Tc-HMDP accumulation revealed calcification in 5 tumors and necrosis in 18. There was calcification in 2 tumors with high uptake, 2 with moderate uptake and 1 with low uptake. These tumors included 4 SCCs and 1 adenocarcinoma.

The pattern of calcification in the tumor was punctate in 2 cases, nodular in 1 case and amorphous in 1 case. The patterns of two patients with high uptake of ^{99m}Tc-HMDP were punctate in one case and nodular in one case. No relationship between the extent of extraosseous ^{99m}Tc-HMDP uptake and the pattern of calcification in the tumor was observed.

A summary of the findings for these 32 patients is shown in Table 1.

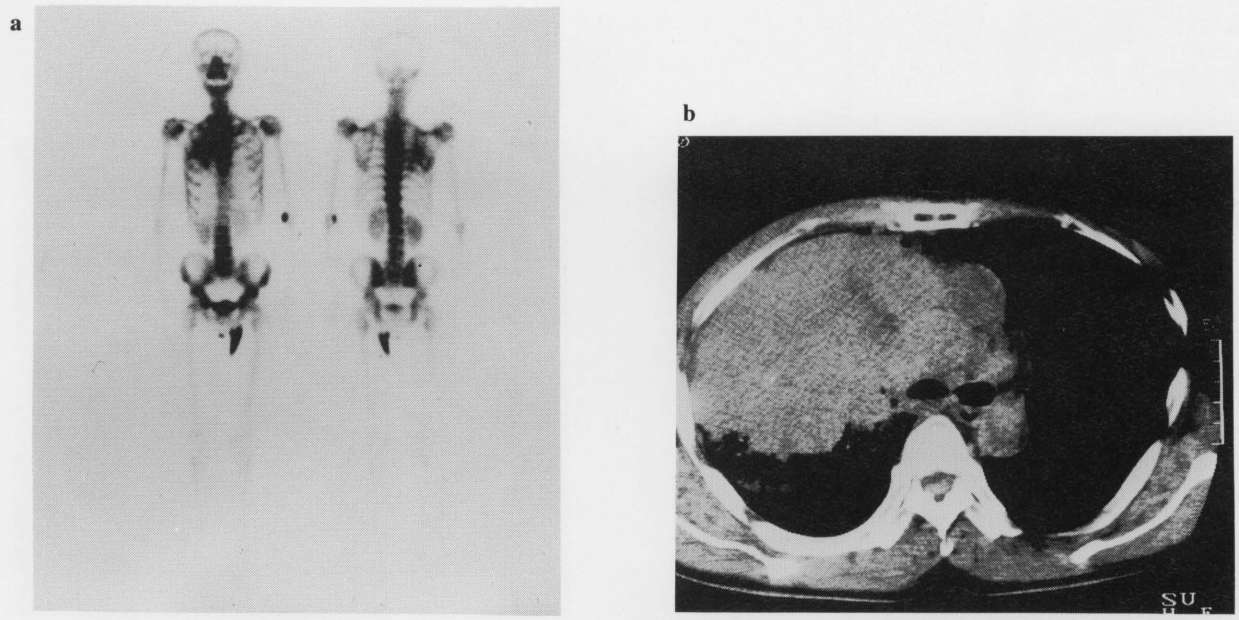

Fig. 2 Case of right lung cancer (SCC) in the upper lobe. Size of the tumor is 8 × 12 cm. a: Anterior and posterior whole body bone scan images. b: Plain CT images of the main tumor. High uptake of ^{99m}Tc-HMDP by a right upper lobe cancer (Anterior and posterior images). Fine punctate calcification in this large tumor was recognized.

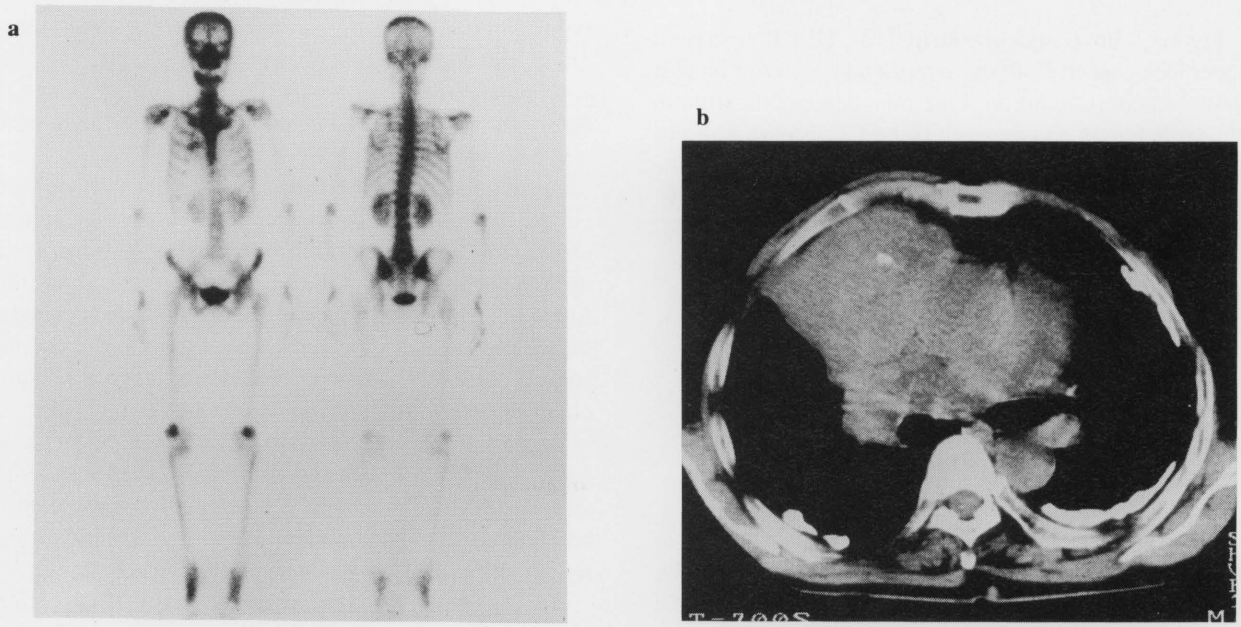

Fig. 3 Case of right lung cancer (SCC) in the upper lobe. Size of the tumor is 10 × 8 cm. a: Anterior and posterior whole body bone scan images. b: Plain CT images of the main tumor. High uptake of ^{99m}Tc-HMDP accumulation by a right upper lobe cancer (Anterior image). Amorphous calcification in the tumor was observed on CT.

The tumors with ectopic accumulation were relatively large, and the mean size was 6 × 6 cm. The relationship between tumor size and the grade of extraosseous uptake is shown in Figure 1. The mean size of the tumors with high uptake was 9 × 10 cm, the size of those with moderate uptake was 6.6 × 6.7 cm, and that of those with low uptake was 5.6 × 5.4 cm.

Tumor necrosis was recognized in 1 case of high uptake, 3 cases of moderate uptake and 14 cases of low uptake.

Examples of high and moderate uptake of ^{99m}Tc-HMDP are shown in Figures 2–4.

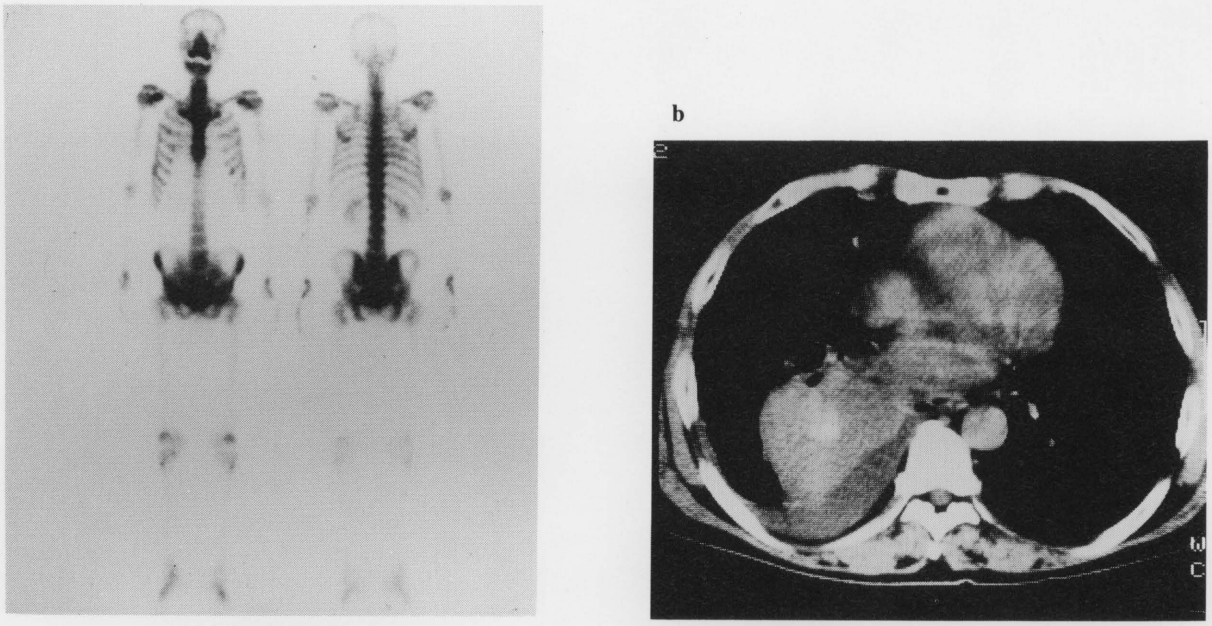

Fig. 4 Case of right lung cancer (Adenocarcinoma) in the apex of lower lobe. Size of the tumor is 9 × 10 cm. a: Anterior and posterior whole body bone scan images. 4b: Plain CT image of the main tumor. Moderate uptake of ^{99m}Tc-HMDP by a right lower lobe cancer (Posterior image). On CT scans, nodular calcification of the tumor was visualized.

Figure 2 shows high uptake of ^{99m}Tc-HMDP by a right upper lobe cancer. Both the anterior and posterior images show high accumulation. Fine punctate calcification in this large tumor was recognized on CT. Figure 3 shows high uptake by another right upper lobe cancer. On the anterior image, abnormal accumulation is marked. Amorphous calcification in the tumor was observed on CT. Figure 4 shows moderate uptake of ^{99m}Tc-HMDP by a right lower lobe cancer.

On the posterior image, abnormal accumulation is recognized. On CT scans, nodular calcification of the tumor was visualized.

DISCUSSION

Our data show that factors such as tumor size, calcification and tumor necrosis influence the ectopic accumulation of ^{99m}Tc-HMDP in lung cancer. Figure 1 shows that ectopic ^{99m}Tc-HMDP accumulation becomes more intense as tumor size increases.

Calcification in the tumor was only visualized in 5 cases, corresponding to 15% of the patients with ectopic ^{99m}Tc-HMDP accumulation.

In Mahoney's mass survey[4] of patients with tumor calcification in lung cancer, 14 out of 20 had tumors more than 5 cm in diameter.

In our series, 80% of the tumors were SCC and 20% were adenocarcinoma, and the patterns of calcification were punctate, amorphous and nodular.

Mahoney reported that tumors included all histological types and that the patterns of calcification were amorphous, punctate and reticular.

Compared to the previous reported frequency of CT detection of calcification in lung cancer,[5–7] our incidence was relatively low.

Another factor in the extraosseous uptake of bone scan agents by the lung cancer was tumor necrosis. In our series, 18 cases of the tumors showing extraosseous uptake had necrosis. On the basis of these data, the following factors may be involved in extraosseous uptake of bone scan agents: 1) Ca ion exchange at the crystal surface in areas of calcification[8] and 2) binding to calcium complex within the cells of necrotic tissue.

Because increased some tumors had no calcification or necrosis on CT, other factors may be involved such as 1) increased calcium metabolic activity,[9] 2) hypervascularity and altered vascular permeability,[10] and 3) binding by tissue hormone or enzyme receptors.[11,12]

The sensitivity of ectopic accumulation of ^{99m}Tc-HMDP was superior to the calcification in the tumor on CT scan. Calcification in the tumor on CT was visualized in 2 case of high uptake of ^{99m}Tc-HMDP. But only 3 cases out of 30 cases of moderate or low uptake of ^{99m}Tc-HMDP showed calcification on CT. ^{99m}Tc-HMDP could accumulate in the tumor in the phase of increased metabolic activity or increased vascular permeability.

If we had sufficient information about the ectopic ^{99m}Tc-HMDP accumulation in lung cancer, we could predict whether these tumors would become necrotic or have a tendency to be calcified in the near future. This would influence the expected efficacy of radiation therapy

or chemotherapy. Intrathoracic ectopic accumulation has also been reported in patients with hypercalcemia,[13] radiation pneumonitis[14] and pleural effusion.[15] In the present series, however, there were no such cases.

We concluded:

1) The incidence of extraosseous accumulation of ^{99m}Tc-HMDP was 7.7% in a series of primary lung cancer (high uptake in 0.5%, moderate uptake in 1.9%, and low uptake in 5.3%).
2) There was no difference in uptake among the various histological types.
3) The tumors with ectopic accumulation were all relatively large.
4) Some of these tumors showed signs of calcification or necrosis, but in some there was no sign of either on CT scans.

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