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Bone scanning in patients with pleural effusion—Experience in 76 cases

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Seventy-six patients with malignant or benign pleural effusion were studied to determine the incidence of accumulation of ^{99m}Tc-MDP in relation to effusion, and reveal the mechanism. Of 76 patients, 46 (61%) were found to have diffuse uptake of ^{99m}Tc-MDP in the hemithorax, with almost the same positive rate in malignant and benign effusions, i.e. 62% and 57%, respectively. Of 46 patients, 32 (70%) showed diffuse, slight accumulation in the hemithorax, and the positive rate had a tendency to be higher with the increase in the effusion volume.

We are convinced that the major mechanism of unilateral intrathoracic accumulation of ^{99m}Tc-MDP in pleural effusion is a passive transudation.

Key words: bone scan, pleural effusion, ^{99m}Tc-MDP, ^{67}Ga citrate

INTRODUCTION

UNILATERAL diffuse intrathoracic accumulation of bone seeking agents is not so uncommon because of the increasing use of these agents in osseous metastasis evaluation. There have been some reports as to the etiology of intrathoracic accumulation.[1–3] Hyperconcentration of ^{99m}Tc bone seeking agents in malignant effusion has also been reported previously.[4–7] No investigator, however, has demonstrated the precise mechanism of accumulation of ^{99m}Tc bone seeking agents in pleural effusion.

In our concern to disclose the mechanism, we reviewed the records of patients with pleural effusion due to miscellaneous diseases, who were referred to us for bone scanning during the previous four years.

The aim of this research is to determine the incidence of accumulation of ^{99m}Tc-MDP in pleural effusion, and to attempt to reveal the mechanism.

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MATERIALS AND METHODS

Bone scintigrams of 76 patients with malignant or benign pleural effusion, who were referred to us for bone scanning from January, 1983 through March, 1987, were analyzed. Of the 76 patients, 41 were male and 35 were female. Age range was 37 to 84 year (mean 59.8 year). All of the patients had definite, clinical and pathological documentation of pleural effusion at either side, when they underwent bone studies. The existence of pleural effusion was detected by radiographs, including CT scan, and/or thoracentesis. The final diagnosis was based on the results of cytology and/or culture or the clinical outcome. Malignant pleural effusion was proved cytologically from pleural fluid samples obtained in thoracentesis or thoracotomy. No patient had received radiotherapy or chemotherapy before the bone studies. Scans were performed approximately 3 hrs after i.v. injection of 740 MBq (20 mCi) of ^{99m}Tc-MDP on a gamma camera.* Both whole body and detailed spot views were taken in each case. We investigated the correlation between the presence of intrathoracic

* Toshiba GCA-401-5 scinticamera and Searle-Siemens LFOV scinticamera.

accumulation of ^{99m}Tc-MDP on bone scan and pleural effusion volume. The volume of pleural fluid was grossly estimated from the chest roentgenograms which were obtained within 1 week of the bone scans and mostly within 3 days. In the 46 out of 76 patients, ^{67}Ga citrate scans were also available for comparison. Both anterior and posterior lung scans were made 48 hrs after i.v. injection of 111MBq (3 mCi) of ^{67}Ga citrate. Posterior spot views were taken in a patient lying prone, with the camera head facing down.

RESULTS

Tables 1, 2 and 3 show the results of our clinical examination. The positive rate of ^{99m}Tc-MDP accumulation in pleural effusion which resulted from miscellaneous diseases is shown on Table 1. Of 76 patients with effusion, 46 (60.5%) were found to have diffuse uptake of ^{99m}Tc-MDP in the hemithorax. The diffuse uptake was demonstrated by bone scan in both malignant and benign effusions, with almost the same positive rate, i.e. 62% and 57%, respectively. Of 46 patients with the diffuse uptake, 32 (69.6%) showed weak activity, 12 (26.1%) showed moderate activity less than that of the rib and 2 (4.3%) showed strong activity equal to the rib uptake (Fig. 1). A definite difference between malignant and benign effusions was not noted in the intensity of uptake.

Table 1 Findings in 76 patients with pleural effusion

Pleural effusion	Diseases	No. of patients	Positive DIU*
Malignant effusion	61 pats—Pleuritis carcinomatosa	61	38 (62%)
Benign effusion	15 pats—Post-thoracotomy	6	2 (33%)
	15 pats—Heart failure	3	3 (100%)
	15 pats—Pulmonary infection	6	3 (50%)
		15	8 (57%)
	Total	76	46 (61%)

*DIU: diffuse intrathoracic uptake

Table 2 Correlation between diffuse intrathoracic accumulation of ^{99m}Tc-MDP and effusion volume estimated from chest roentgenogram

Chest roentgenogram finding	Diffuse intrathoracic uptake	
	Present	Absent
Slight obliteration of the costphrenic angle	36% (8/22)	64% (14/22)
Opacification less than 1/3 of the hemithorax	55% (11/20)	45% (9/20)
Opacification more than 1/3 of the hemithorax	79% (27/34)	21% (7/34)

Table 3 Correlation between Tc-99m MDP scan and Ga-67 citrate scan in patients with pleural effusion

Malignant effusion (40 cases)	Positive MDP scan (31 cases)	Positive Ga-67 scan	18 (58%)
		Negative Ga-67 scan	13 (42%)
	Negative MDP scan (9 cases)	Positive Ga-67 scan	0 (0%)
		Negative Ga-67 scan	9 (100%)
Benign effusion* (6 cases)	Positive MDP scan (5 cases)	Positive Ga-67 scan	4 (80%)
		Negative Ga-67 scan	1 (20%)
	Negative MDP scan (1 case)	Positive Ga-67 scan	0 (0%)
		Negative Ga-67 scan	1 (100%)

*; Heart failure 3 cases, Pneumonia 2 cases, Post-thoracotomy 1 case

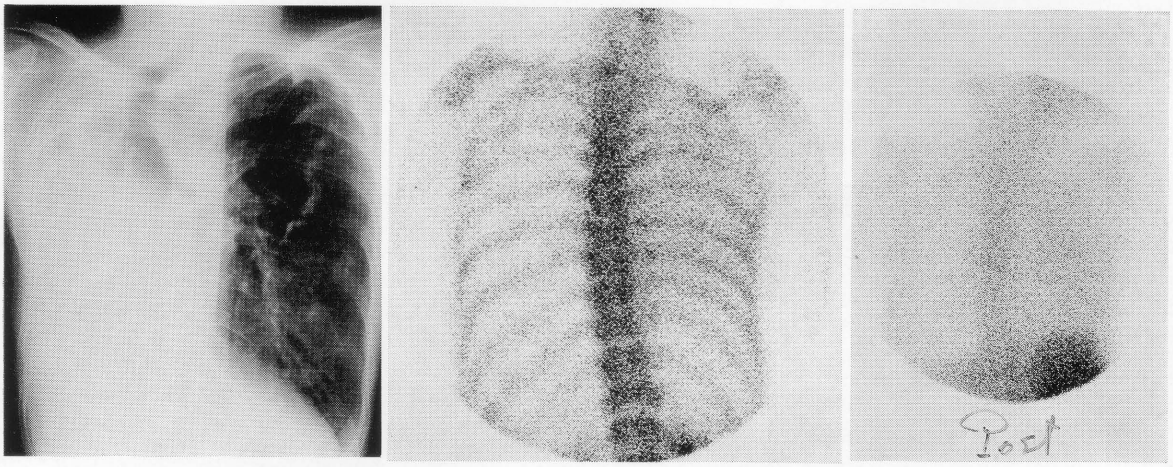

Fig. 1 A 60-year-old female with old pulmonary tuberculosis and mitral regurgitation. She was admitted to the hospital with dyspnea and right omalgia. Chest radiograph (Left) shows opacification in the entire right hemithorax. Posterior view from a bone scan (Middle) demonstrates slightly increased accumulation of ^{99m}Tc-MDP in the right hemithorax. ^{67}Ga scan (Right) also depicts slight uptake in the right hemithorax. She was proven to have benign pleural effusion due to cardiac failure, and it disappeared following treatment with diuretics and digitalization.

The positive rate of uptake tended to be higher with the increase in effusion volume estimated from chest roentgenogram (Table 2).

Of 36 patients with the uptake of ^{99m}Tc-MDP, 22 (61%) similarly showed intrathoracic, diffuse uptake of ^{67}Ga (Table 3). Of 10 patients without the uptake of ^{99m}Tc-MDP, none showed uptake of ^{67}Ga.

DISCUSSION

Diffuse increased radioactivity in the thoracic region occasionally has been observed in ^{99m}Tc phosphate bone studies. Non-osseous uptake by skeletal agents is a well-known fact and some investigators have reported diffuse intrathoracic accumulation of skeletal agents in several disease states such as metastatic calcification,[8–10] pleural effusion,[4–7] radiation pneumonitis,[11] alveolar microlithiasis[12] and fibrothorax.[13] Levy and Park[14] reported that unilateral thoracic soft-tissue accumulation of bone agents was present in 60 of 130 (46%) of patients with lung cancer. In that study, they emphasized that radiation therapy for lung tumors was the most significant of the factors studied in unilateral soft-tissue uptake of bone agents in the thorax of patients with lung cancer. But our patient population did not receive any radiotherapy.

The precise mechanism of phosphate accumulation in effusion remains to be clarified, although some speculations as to its mechanism have been reported.[4–7] Disruption or altered capillary permeability in the pleura is considered as the most likely mechanism in malignant effusion. With an inflammatory change or due to a hypervascular tumor in the pleura, increased vascularity could occur in that area. Metabolic effects exerted by tumor cells might increase the amount of calcium and phosphorus in effusion. Collagen formation and activated phosphatase in effusion might also be related to the localization of ^{99m}Tc-MDP.[13]

In our study, ^{99m}Tc-MDP accumulation in pleural effusion was noted not only in patients with malignant effusion, but also with benign effusion, with almost the same positive rate. Especially there was a diffuse uptake of the radiotracer in all of 3 patients with effusion due to congestive heart failure, and also 2 patients with thoracotomy. These effusions are so-called transudates, not exudates. About 70% of our subjects showed slight or vague accumulation of ^{99m}Tc-MDP in the hemithorax. The positive rate of accumulation had a tendency to be higher with the increase in intrathoracic effusion volume. Patients with a pleural effusion less than 300 m*l* did not show diffuse intrathoracic uptake on bone scan because up to 300 m*l* of fluid is not apparent in the usual upright chest X-ray (Table 2). These results probably suggest that a simple effusion is a principal factor in the diffuse intrathoracic accumulation of ^{99m}Tc-MDP.

As to the comparison between ^{67}Ga citrate and ^{99m}Tc-MDP, of 46 cases, 22 (47.8%) showed diffuse, slight accumulation of both agents, and 10 (21.7%) showed accumulation of neither ^{67}Ga nor ^{99m}Tc-MDP. This correlation between ^{67}Ga and ^{99m}Tc-MDP seems to suggest that ^{67}Ga accumulation in effusion also might be partly due to simple diffusion

into the intrapleural space. Hatfield[15] published an article on gallium accumulation in the ipsilateral hemithorax as the effect of previous thoracic surgery, which seems to endorse our results.

From these results, we suggest that, once ^{99m}Tc-MDP is distributed throughout the extracellular compartment, in the third space after i.v. injection, it passively transudes into the intrapleural space and is cleared slowly from the congested intrathoracic space. Transudates including ^{99m}Tc-MDP are those fluids which occur in response to an increase in hydrostatic pressures in the capillaries, a decrease in the oncocytotic pressure of plasma, a decrease in intrapleural pressure, or a combination of these factors.

In conclusion, while it is difficult to define a single mechanism which accounts for all of the cases we studied, we are convinced that, in patients with malignant or benign pleural effusion, passive diffusion of ^{99m}Tc-MDP along with effusion and its slow clearance from the congested intrathoracic space play a major role in diffuse intrathoracic accumulation in bone scan.

REFERENCES

1. Silberstein EB, McAfee JG: Differential diagnosis in nuclear medicine. New York, McGraw-Hill, 1984, p 303
2. Datz FL: Gamuts in nuclear medicine. Norwalk, Appleton-Century-Crofts, 1983, pp 107–108
3. Amico S, Lucas P, Diebold MD, et al: Metastatic calcification in the thyroid gland demonstrated on bone scan in a patient with primary hyperparathyroidism. *J Nucl Med* 27: 373–376, 1986
4. Siegel ME, Walker WI JR, Campbell JL, I: Accumulation of ^{99m}Tc diphosphonate in malignant pleural effusions. *J Nucl Med* 16: 883–885, 1975
5. Aprile C,Bernaldo G, Carena G,et al: Accumulation of ^{99m}Tc Sn pyrophosphate in pleural effusion. *Eur J Nucl Med* 3: 219–222, 1978
6. Lamki L, Cohen P, Driedger A: Malignant pleural effusion and Tc-99m MDP accumulation. *Clin Nucl Med* 7: 231–233, 1982
7. Goldstein HA, Gefter WB: Detection of unsuspected malignant pleural effusion by bone scan. *Clin Nucl Med* 9: 556, 1984
8. Cohen AM, Maxon HR, Goldsmith RE, et al: Metastatic pulmonary calcification in primary hyperparathyroidism. *Arch Int Med* 137: 520–522, 1977
9. Van Antwerp JD, O'Mara RE, Pitt MJ, et al: Technetium-99m-diphosphonate accumulation in amyloid. *J Nucl Med* 16: 238–240, 1975
10. Wychank S: ^{99m}Tc-methylene diphosphonate lung uptake in mixed small and large cell lymphoma. Eur *J Nucl Med* 7: 47–48, 1982
11. Sarreck R, Sham R, Alexander LL, et al: Increased ^{99m}Tc-pyrophosphate uptake with radiation pneumonitis. *Clin Nucl Med* 4: 403–404, 1979
12. Brown ML, Swee RG, Olson RJ, et al: Pulmonary uptake of ^{99m}Tc diphosphonate in alveolar microlithiasis. *Am J Roentgenol* 131: 703–704, 1978
13. Ravin CE, Hoyt TS, DeBlanc H: Concentration of ^{99m}Technetium polyphosphate in fibrothorax following pneumonectomy. *Radiology* 122: 405–408, 1977
14. Levy HA, Park CH: Unilateral thoracic soft-tissue accumulation of bone agent in lung cancer. *J Nucl Med* 28: 1275–1278, 1987
15. Hatfield MK, MacMahon H, Martin WB, et al: The effect of previous thoracic surgery on gallium uptake in the chest. *J Nucl Med* 28: 1831–1834, 1987