
Technetium-99m-Methylene Diphosphonate (MDP) Uptake in a Sympathetic Effusion: An Index of Malignancy and a Review of the Literature

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We report a patient with a sympathetic pleural effusion secondary to T-cell lymphoma that accumulated the bone imaging agent, Technetium-99m-methylene diphosphonate (^{99m}Tc -MDP). This case is significant in that malignant cells were not present on three cytologic examinations of the pleural fluid or multiple pleural biopsies. We also present a review of the published literature on pleural effusions that accumulate bone tracers. We conclude that pleural effusions that accumulate ^{99m}Tc -MDP should be considered malignant or secondary to a malignancy and further work-up is essential even if the cytologic exam of the pleural fluid is unremarkable.

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CASE REPORT

A 74-yr-old white male non-smoker, with an unremarkable past medical history presented with a 24-pound weight loss over the past 6 mo. Physical exam revealed a large mass in the left upper quadrant. The chest radiograph demonstrated a left pleural effusion. The patient underwent a thorough work-up, including three pleural fluid aspirations, pleural biopsies, bronchoscopy, and bone marrow biopsy. All the tests revealed no evidence of malignancy.

A bone scan was performed 4 h after the i.v. administration of 20 mCi (740 MBq) of technetium-99m-methylene diphosphonate (^{99m}Tc -MDP) using a large field of view Anger camera equipped with a general-purpose collimator. The bone scan demonstrated ^{99m}Tc -MDP accumulation in a left pleural effusion (Figs. 1 A-B). Computed tomography of the abdomen revealed a 9×7 cm mass in the left upper quadrant abutting the diaphragm and a 4×4 cm mass in the left cardiophrenic

angle (Fig. 2). The masses were biopsied and found to be T-cell lymphoma.

DISCUSSION

Bone scanning agents have been observed to accumulate in malignant pleural effusions (1-5) and, in one report, in a non-malignant pleural effusion (6). The currently reported case is of interest because of the accumulation of ^{99m}Tc -MDP in a sympathetic pleural effusion secondary to lymphomatous masses in the left upper quadrant of the abdomen and in the left cardiophrenic angle, abutting the pleural surface (Fig. 2). Malignant cells have been identified by cytology of the pleural aspirate in 14 out of 15 previously reported cases of pleural effusions that demonstrated uptake of ^{99m}Tc -MDP (1-5). In this case, no malignant cells were identified in the pleural fluid from three different aspirations and multiple pleural biopsies. Specifically, cytologic examination of the pleural fluid demonstrated benign reactive changes. The effusion was grossly bloody (20,000 RBCs) and exudative (total protein 4.69 g/dl and LDH 590 u/l) on initial examination. The absence of malignant cells may be important in helping to further elucidate the mechanism of ^{99m}Tc -MDP uptake in malignant effusions.

Table 1 summarizes a review of reported cases in which ^{99m}Tc -MDP has accumulated in pleural effusions. Of the 15 reported cases, 14 were malignant. Prior to 1988, all pleural effusions that accumulated ^{99m}Tc -MDP were proven to be of malignant origin by cytology. In 1988, Babel et al. (6) published a single case report in which an effusion accumulated ^{99m}Tc -MDP with no demonstrable evidence of malignant cells in the pleural fluid aspirate.

The mechanism by which ^{99m}Tc -MDP accumulates in pleural effusions is not well understood. Technetium-99m MDP is a large, non-ionic molecule which does not freely diffuse into the pleural space (7). Siegel et al. (2) demonstrated that more than 99% of the radioac-

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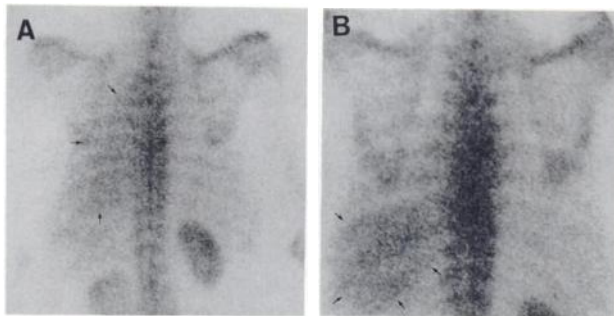


FIGURE 1

(A) Supine posterior image of the thorax from the ^{99m}Tc -MDP bone scan after a 4-hr delay demonstrates diffuse, increased soft-tissue activity (small arrows) of the tracer in the left hemithorax. (B) Upright posterior image of the thorax on the bone scan demonstrates the tracer activity to localize in the lower one-third of the thoracic cavity (small arrows). This is evidence for uptake within the pleural effusion that has redistributed (in the upright position).

tivity in malignant effusions was found in the non-cellular, fluid component. Our case supports this finding, since no malignant cells were found in the pleural fluid. Furthermore, Siegel et al. (2) determined that the radioactivity in the effusion was in the form of ^{99m}Tc -MDP and not free pertechnetate.

Several mechanisms by which ^{99m}Tc -MDP accumulates in malignant effusions have been postulated, one of which suggests disruption of pleural permeability by tumor involvement (3). Our case supports this hypothesis, since the lymphomatous masses in the left upper quadrant and the cardiophrenic angle were adjacent to the pleural surface (Fig. 2). However, our case suggests that tumor involvement within the pleural space or invasion of the pleura is not a prerequisite for accumulation of ^{99m}Tc -MDP, as the pleural effusion, cytology, and multiple pleural biopsies could identify no

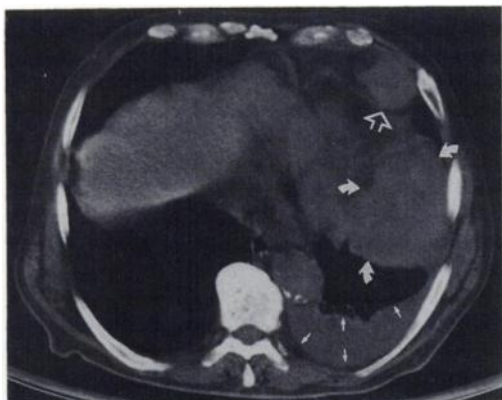


FIGURE 2

Selected 10-mm thick image from a computed tomogram of the abdomen, demonstrating a 9 × 7 cm mass (solid, curved arrows) just inferior to the left hemidiaphragm; a 4 × 4 cm mass (open arrow) in the left cardiophrenic angle; and a left pleural effusion (small arrows).

TABLE 1
Review of Published Reports on Effusions that Concentrate ^{99m}Tc -MDP

| Study | No. of patients | Type of effusion | Type of malignancy |
|--------------------------------|-----------------|------------------|--|
| Goldstein et al. 1984 (Ref. 1) | 1 | Malignant | Breast cancer |
| Siegel et al. 1975 (Ref. 2) | 2 | Malignant | Lung cancer Breast cancer |
| Lamki et al. 1982 (Ref. 3) | 2 | Malignant | Breast cancer Breast cancer |
| Shih 1985 (Ref. 4) | 6 | Malignant | Bronchogenic cancer—all pts. |
| Kida et al. 1984 (Ref. 5) | 3 | Malignant | Gastric cancer Breast cancer Lung cancer |
| Babbal et al. 1988 (Ref. 6) | 1 | Non-malignant | |

malignant cells. It is likely that the mere presence of a tumor mass in close contact with the pleural surface can disrupt the permeability dynamics of the pleura, allowing for radiotracer accumulation in the effusion. The altered permeability may be due to a direct mechanical effect by the tumor on the pleura, the host's response to the tumor, or metabolic effects of the tumor.

The mechanism of ^{99m}Tc -MDP uptake in malignant pleural effusion remains undetermined. The process probably involves a combination of factors, although the primary contributor is likely to be a disruption of pleural permeability. However, this report suggests that tumor invasion of the pleura and pleural space is not a requirement for concentration of ^{99m}Tc -MDP in the effusion. Reports of benign pleural effusions accumulating ^{99m}Tc -MDP are rare (6).

What a malignancy does to the pleural surface to permit the accumulation of ^{99m}Tc -MDP that other etiologies (i.e., infection, congestive heart failure, etc.) for pleural effusion do not do, remains to be answered. We offer altered permeability of the pleura due to mechanical effects by the tumor, the host's response to the tumor, and/or metabolic effects of the tumor, as possible explanations. The answer may also lie in patient selection. The majority of bone scans performed at our institution are to evaluate for metastatic disease. We do not routinely perform bone scans on patients with parapneumonic effusions or congestive heart failure. A large series of patients with pleural effusions of various etiologies needs to be studied to address this patient selection bias.

This report and the current literature lead us to conclude that a thorough search for malignancy should be undertaken when a pleural effusion accumulates ^{99m}Tc -MDP. As this case demonstrates, a malignancy may be present even when the cytologic examination of the pleural fluid is negative.

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