ACCUMULATION OF ^{99m}Tc-DIPHOSPHONATE IN MALIGNANT PLEURAL EFFUSIONS: DETECTION AND VERIFICATION

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Increased accumulation of radioactivity was observed in two cases of malignant pleural effusions during the performance of routine bone scans with ^{99m}Tc-diphosphonate. This previously unreported finding was verified both qualitatively and quantitatively by appropriate scanning and laboratory techniques.

Technetium-99m-diphosphonate as well as other closely related compounds have recently been reported to accumulate in extraosseous tissues (*1–3*). Concentrations in various soft-tissue malignancies including: astrocytoma, lymphoma, neurofibroma, and breast carcinoma have been noted. Technetium-99m-diphosphonate has also been shown to accumulate in cartilagenous tissues (*4*). This report describes the accumulation of ^{99m}Tc-diphosphonate in two cases of malignant pleural effusions, a finding that differs from previous reports in that it does not necessarily involve bone or soft tissue. The finding was verified in one patient both qualitatively and quantitatively.

CASE REPORTS

Case 1. A 52-year-old man with carcinoma of the left main stem bronchus had a routine bone scan performed in the supine position with a dual-probe rectilinear scanner 2½ hr after intravenous administration of 15 mCi of ^{99m}Tc-diphosphonate. The radionuclide scan was normal except for the diffuse activity that was observed in the left posterior hemithorax that was not related to any specific bony structures (Fig. 1). At that time a chest roentgenogram demonstrated evidence of a left pleural effusion. Thoracentesis yielded approximately 150 cc of effusion and contained malignant cells.

Case 2. A 50-year-old woman who had had a resection for carcinoma of the right breast was referred for a routine bone scan. The skeleton appeared normal but on the posterior view a diffuse accumulation of radioactivity was observed in the left hemithorax (Fig. 2). A chest roentgenogram revealed a left pleural effusion. Approximately 30 hr after the first study the patient again was administered ^{99m}Tc-diphosphonate and a second rectilinear bone scan of the thorax was performed. The diffuse uptake in the left hemithorax was still present (Fig. 3A). A

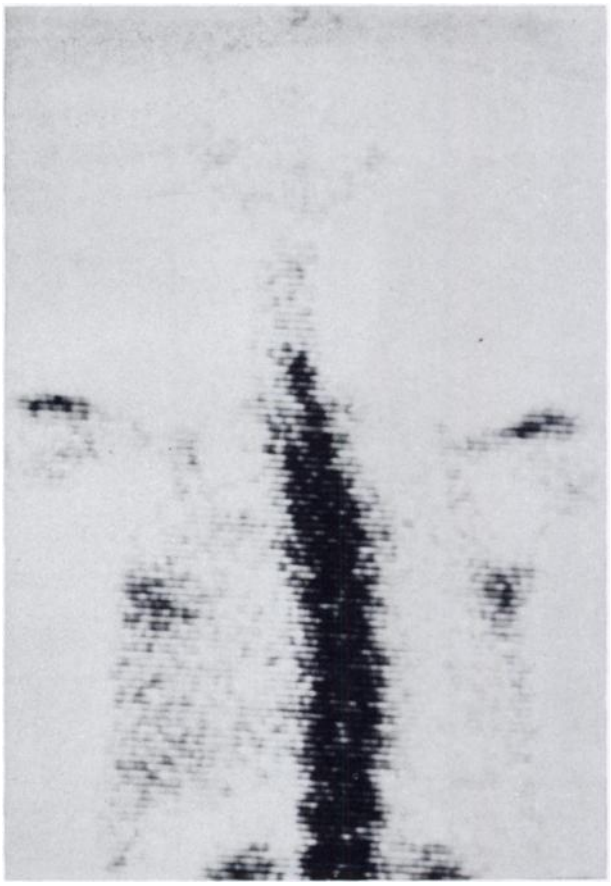

FIG. 1. Case 1. Posterior ^{99m}Tc-diphosphonate bone scan demonstrates diffuse increased radioactivity in left hemithorax site of malignant pleural effusion.

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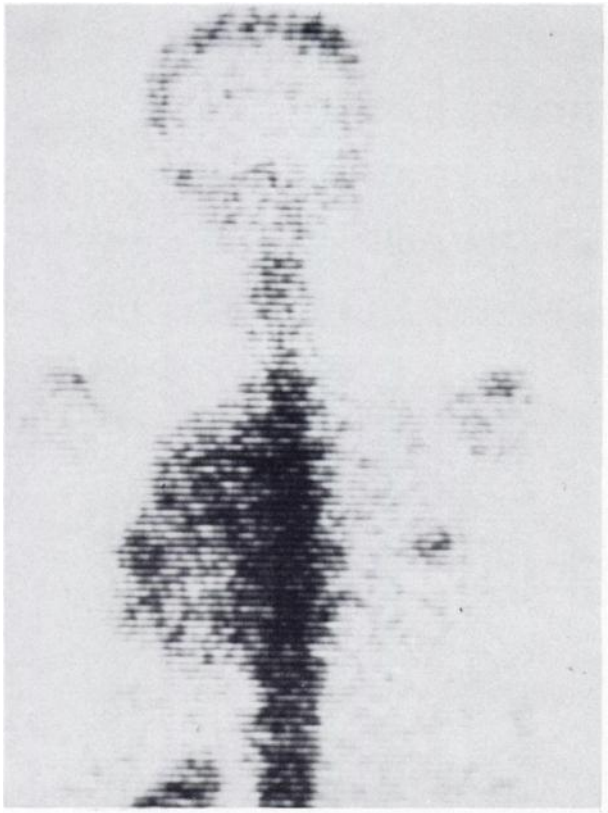

FIG. 2. Case 2. Posterior ^{99m}Tc-diphosphonate bone scan demonstrates diffuse increased radioactivity in left hemithorax where patient had malignant pleural effusion.

thoracentesis yielded approximately 2 liters of fluid containing malignant cells. An aliquot of the effusion was separated by centrifugation into the cellular and noncellular components and the amount of radioactivity per unit volume was determined on the supernatant part of the effusion, the cellular portion, and the total fluid. Blood samples were obtained at the time of the thoracentesis and radioactivity per unit volume was measured. By means of standard thin-layer chromatographic and analytical techniques, the chemical and radiochromatographic properties of the perfusion were also determined. A rectilinear scan of the thorax was performed (Fig. 3B) following thoracentesis.

RESULTS

In Case 2 the malignant effusion contained approximately three times the radioactivity per unit volume as that of the whole blood, and more than 99% of the radioactivity in the malignant effusion was found in the noncellular, fluid component (Table 1). Chromatographically, more than 99% of the radioactivity in the malignant effusion was found at the origin with essentially no activity at the solvent front. As a control, a drop of free pertechne-

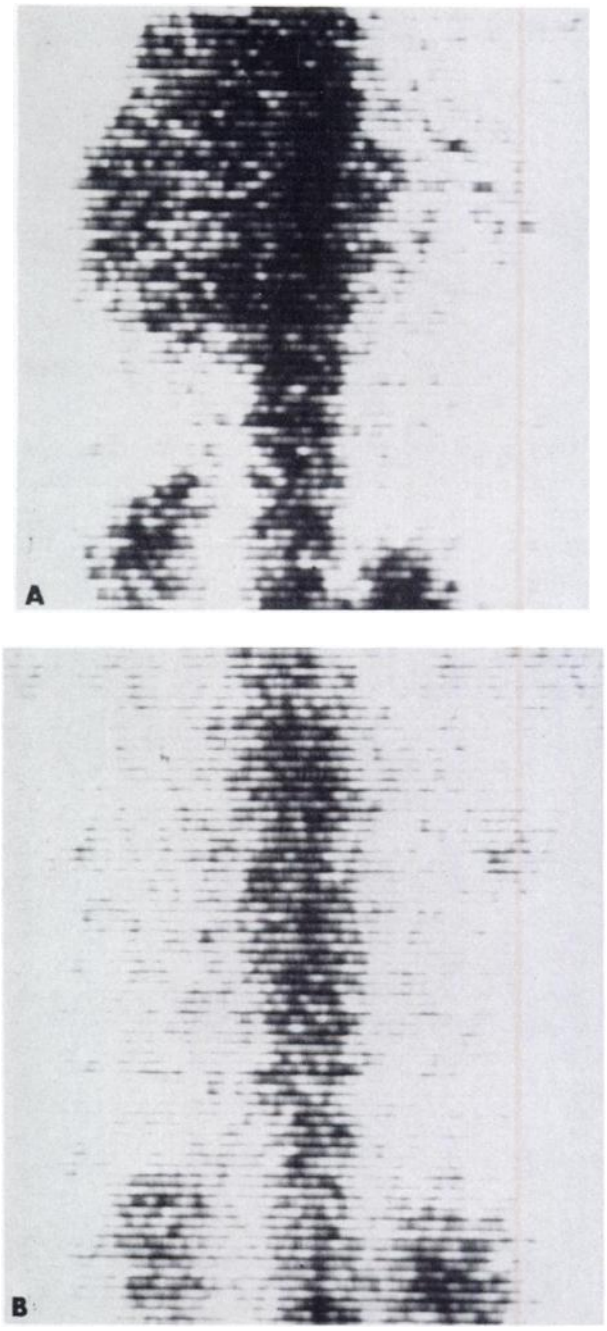

FIG. 3. (A) Repeat posterior bone scan of patient in Fig. 2 done before thoracentesis confirms increased radioactivity in left hemithorax. (B) Posterior bone scan done immediately after thoracentesis demonstates absence of previously observed increased radioactivity in left hemithorax.

TABLE 1. RADIOACTIVITY IN COMPONENTS OF MALIGNANT PLEURAL EFFUSION AND BLOOD

Sample	Activity per milliliter
Total unseparated effusion	17 ± 0.04 nCi
Noncellular component of effusion	18 ± 0.06 nCi
Cellular component of effusion	80 ± 4.1 $\mu\mu$Ci
Whole blood	6 ± 0.03 $\mu\mu$Ci

tate was chromatographed and more than 99% of the activity was located at the solvent front. Chemical analysis of the effusion, including phosphorus (3.7 mg/dl), calcium (7.9 mg/dl), alkaline phosphatase (17 IU/dl), acid phosphatase (0.3 IU/dl) and total protein (4.9 gm/dl), was similar to that found in blood. The pre- and post-thoracentesis scans verified qualitatively that the abnormal diffuse accumulation of radioactivity in the left hemithorax was in the malignant pleural effusion.

DISCUSSION

A review of the literature shows that no evidence of accumulation of ^{99m}Tc-diphosphonate or any of its closely related phosphate compounds has been reported in malignant pleural effusions. We have demonstrated accumulation of radioactivity within an effusion and initial observations include the following: (A) the radiopharmaceutical will accumulate in malignant pleural effusions; (B) the accumulating radiopharmaceutical is not free pertechnetate; and (C) the radiopharmaceutical is almost exclusively in the noncellular, fluid component of the effusion.

Additional investigations are necessary to define further the chemical characteristics of the accumulating radiopharmaceutical and the etiologic factors responsible for its accumulation and to determine the specificity, and thus the clinical significance, of this finding. Current investigations with ^{99m}Tc-diphosphonate in patients with both malignant and benign pleural effusions suggest a specificity of this accumulation for malignant pleural effusions. However, at this time the number of studies is too small to be conclusive.

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