ACCUMULATION OF ^{99m}Tc-POLYPHOSPHATE IN TWO SQUAMOUS CELL CARCINOMAS OF THE LUNG: CASE REPORT

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Technetium-99m-polyphosphate was found to accumulate in two squamous cell carcinomas of the lung. In one case, microscopy and electron microscopy failed to demonstrate calcification in the tumor. Possible mechanism(s) of accumulation of polyphosphate in nonosseous tissues was reviewed.

Since the introduction of ^{99m}Tc-phosphate bone-scanning agents, there has been an increasing number of reports of the extraosseous soft-tissue accumulation of this family of radionuclides. A few of these reports have shown localization of tracer in tissue presumed or demonstrated to contain pathologic calcification or heteroplastic bone formation. Many, however, have reported uptakes in areas where no calcium or bone tissue could be found by roentgenography or microscopic examination. The mechanism(s) of accumulation in these cases has not been delineated. In the present report of two patients, there was localization of ^{99m}Tc-polyphosphate in squamous cell carcinoma of the lung that did not have demonstrable calcification. To our knowledge, no case of noncalcified primary squamous cell carcinoma of the lung has previously been shown to concentrate ^{99m}Tc-polyphosphate.

CASE REPORTS

Case 1. A 60-year-old white male was admitted to the hospital with an 8-month history of progressive cough. Two weeks prior to admission he developed hemoptysis. He had been a heavy smoker for most of his life and had worked in an asbestos-roofing factory for many years.

Laboratory data on admission included normal serum calcium and phosphorous. A radiograph of the chest (Fig. 1A) and chest tomograms showed a mass in the left hilum partially occluding the left main

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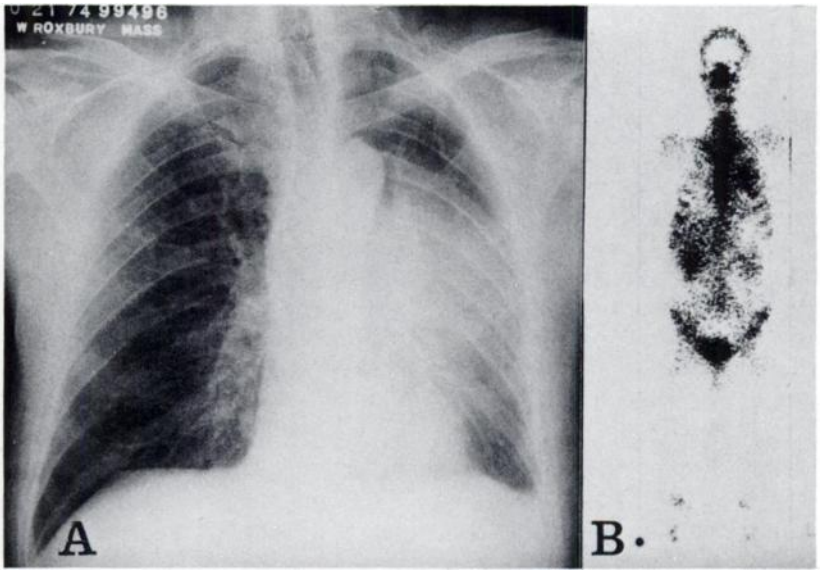

FIG. 1. (A) Chest radiograph shows tumor mass in left hilar region; and (B) anterior ^{99m}Tc-polyphosphate bone scan shows accumulation of isotope in area of tumor mass seen on chest x-ray.

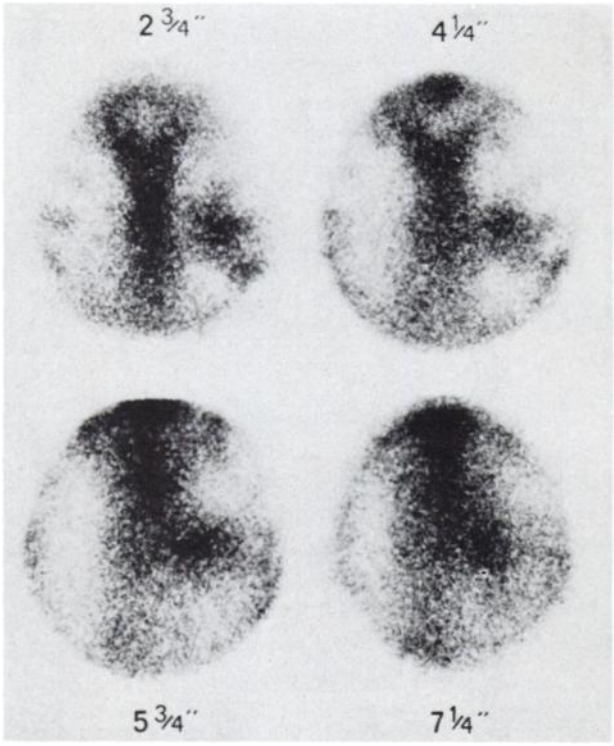

FIG. 2. Anterior scintigraphic tomograms of chest obtained with Searle Radiographics Pho/Gamma Tomocamera System show progressively increased accumulation of tracer in left lung below level of anterior ribs. Numbers refer to depth in inches below face of collimator.

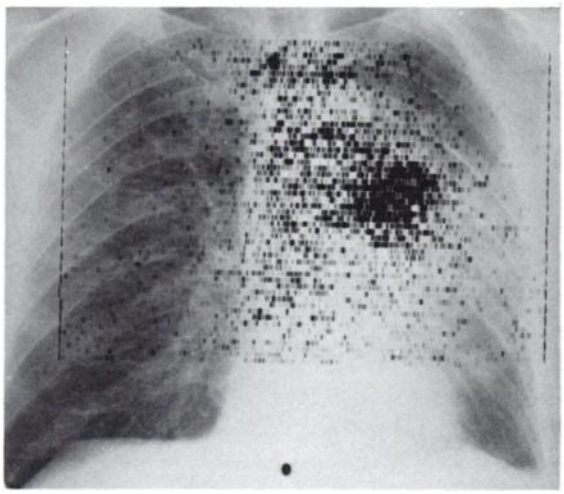

FIG. 3. Anterior ^{67}Ga-citrate scan taken 5 days following intravenous injection shows accumulation in region of tumor mass seen on chest x-ray.

stem bronchus. There was no evidence of calcification by roentgenograms.

The ^{99m}Tc-polyphosphate bone scan showed increased accumulation of the radiopharmaceutical in the area of the left hilar mass (Fig. 1B). Scintigraphic tomograms showed that the accumulation of isotope was within the lung and not in the overlying bony structures (Fig. 2). A ^{67}Ga-citrate scan also showed concentration in the same area (Fig. 3). Biopsy material obtained by bronchoscopy revealed a squamous cell carcinoma, and the patient underwent a left pneumonectomy.

The surgery revealed a large tumor in the left upper lobe. On sectioning and microscopic examination the tumor was seen to have a large central necrotic region with much hyperemia in the surrounding viable tumor and normal lung parenchyma. A careful search of multiple tissue sections stained with hematoxylin and eosin failed to demonstrate the presence of calcium deposits in the tumor or surrounding area. A von Kossa stain did not show any microscopic calcification in the tumor. Further examination of the tissue by electron microscopy did not reveal any evidence of crystalline-appearing deposits.

Case 2. A 69-year-old white male came to the hospital with a history of dyspnea and hemoptysis. Physical examination revealed enlarged left cervical nodes. Chest x-ray showed a small density near the left hilum. A bronchoscopic biopsy was diagnosed as squamous cell carcinoma. The patient was treated with radiation and did well. Eight months later he developed pain on the left side of the chest associated with dyspnea and a dry cough. Chest x-ray and tomograms showed progressive enlargement of the left hilar lesion, which was now cavitated. A ^{99m}Tc-polyphosphate bone scan demonstrated concentration in the diseased area seen on the chest x-ray. Scintigraphic tomograms showed that the activity was within the lung and did not involve overlying bony structures. The remainder of the metastatic workup was negative and the patient was treated again with radiation.

DISCUSSION

Extraosseous accumulation of phosphate bone-seeking radionuclides has been reported in a variety of noncalcified soft tissues. These include cerebral infarcts (*1,2*), soft-tissue abscess (*3*), breast tumors (*3,4*), and metastatic adenocarcinoma of the rectum (*5*). There has been much speculation as to the mechanism(s) involved.

Many of the reported instances of noncalcified soft-tissue uptake of phosphate bone-scanning agents involved tissues with areas of necrosis or tissues such as breast and colorectal carcinoma that are prone to pathologic calcification and heteroplastic bone formation (*6–8*). Silberstein (*9*) has reported that, at least for ^{99m}Tc-labeled diphosphonate, tracer deposition correlates with increased molar calcium and phosphorus content of the tissues studied. On the basis of what is known about the mechanism

of uptake of bone-scanning agents by the skeletal system, it seems reasonable, therefore, to postulate that ion exchange between intracellular calcium phosphate and phosphate bone-scanning agents is responsible for the uptake by soft tissue. Thus, an abnormal scan may occur even though a slight increase in calcium content of the tissue is undetectable by radiographic or histologic examination. Positive myocardial scintigrams, for example, which occur in patients with acute myocardial infarction, and which are obtained using phosphate bone-scanning agents, are thought to be due to the exchange of the tracer for the increased calcium present in irreversibly damaged myocardial cells (*10*). As with skeletal uptake, soft-tissue accumulation of tracer may correlate with regional blood flow (*11*).

In our two cases no calcification in the area of the tumor was seen by x-ray, and in the case examined histologically by light and electron microscopy no calcification could be detected. It is possible, however, that an increased concentration of calcium ions was present in the tumor cells, or at least in the dead or degenerating areas of the tumor, and that increased blood flow, suggested in one case by the hyperemic zone around the area of central necrosis, caused the increased concentration of ^{99m}Tc-polyphosphate in the tumor. As suggested by Silberstein (*9*), it would aid in further clarification of the mechanism(s) of soft-tissue accumulation of bone-scanning agents to actually measure the molar calcium and phosphorus content of the tissue.

Both instances of soft-tissue uptake of bone-scanning agents described in this paper involved squamous cell carcinoma of the lung. Whether this association has prognostic significance perhaps deserves further investigation.

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