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Increased Thallium-201 Uptake in Collapsed Lung: A Pitfall in Scintigraphic Evaluation of Central Bronchogenic Carcinoma

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This study evaluated whether ^{201}Tl scintigraphy can differentiate a central bronchogenic cancer from a distal collapse consolidation. **Methods:** Nine patients with squamous carcinoma with collapse confirmed by surgery and pathology were included. All patients underwent SPECT 1 hr after an intravenous injection of 3 mCi of ^{201}Tl. Four-hour delayed SPECT was performed in five of the nine patients. The thallium activity in tumor and collapse was visually assessed on the basis of the pathologic findings. The specimens were prepared to have the same orientation and level with the SPECT image. **Results:** The tumor activity appeared higher than that of the collapse in four patients, equal in three patients and lower in two patients. Both collapsed lung with and without superimposed inflammation also showed increased thallium activity. Delayed SPECT aided in tumor detection within a collapsed lung in only two of the five patients. **Conclusion:** Our study illustrates the need for caution in the interpretation of thallium scintigraphy in patients with central bronchogenic cancer and distal collapse.

Key Words: lung cancer; thallium-201; SPECT

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Thallium-201-chloride has been described as a positive indicator for lung neoplasms (*1–3*). A recent comparative study of ^{201}Tl and ^{67}Ga-citrate in 38 patients with proven primary lung cancer demonstrated that ^{201}Tl is superior to ^{67}Ga in the detection of the primary tumor and metastasis in the mediastinum (*4*). However, these studies were undertaken in patients with solitary pulmonary nodule (SPN) or isolated tumor masses. Frequently central bronchogenic cancer accompanies distal collapse or pneumonitis which may obscure the primary tumor causing difficulty in assessing tumor extent. Differentiation of the primary tumor from atelectasis is important for deciding whether to perform bronchoscopic biopsy or percutaneous needle aspiration biopsy. Although contrast-enhanced CT or T2-weighted MRI may be helpful in the differentiation (*5*), this is not always possible. Therefore, we performed SPECT studies in patients with central bronchogenic cancer with post-obstructive pneumonia to evaluate whether ^{201}Tl SPECT is useful in the detection of a tumor mass within a collapsed lobe. The radioactivity within the tumor and obstructive pneumonia was assessed visually and compared to pathologic findings from operative specimens prepared from the same level and in the same orientation to those of SPECT images.

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MATERIALS AND METHODS

Nine patients (8 male, 1 female; age 50–75 yr) with central squamous carcinoma with distal collapse or consolidation were included in this study. Pneumonectomy or lobectomy was performed in all of the patients within 1 wk after ^{201}Tl SPECT. No specific treatment for atelectasis or bronchogenic cancer was attempted before surgery. Multiple pathologic slices were obtained to match the level and orientation of SPECT images. The tumor masses were evaluated in regard to the size, differentiation and presence of necrosis. Collapsed distal lung parenchyme was evaluated as to whether there was associated inflammation.

A SPECT study of the chest was obtained 1 hr after an intravenous injection of 111 MBq (3 mCi) of ^{201}Tl on a single-headed (Siemens Orbiter 7500, Hoffman Estates, IL) or a dual-headed gamma camera (ADAC, Milpitas, CA) equipped with a high-resolution, low-energy parallel-hole collimator. Sixty-four projections with an acquisition time of 40 sec/view were acquired in 64 × 64 matrices with a 5.6-degree of angular increment. The images were reconstructed with a filtered backprojection method using a Butterworth filter (cut-off frequency of 0.35 cycle/cm at order no. 5). Attenuation correction was not performed. Delayed SPECT was performed in five of nine patients 4 hr later. The thallium activity of the tumor and collapse was visually assessed and scored as follows:

Grade+: intensity similar to that of the contralateral lung.
Grade++: intensity higher than that of the contralateral lung but less than that of the heart.
Grade+++: intensity similar to that of the heart.

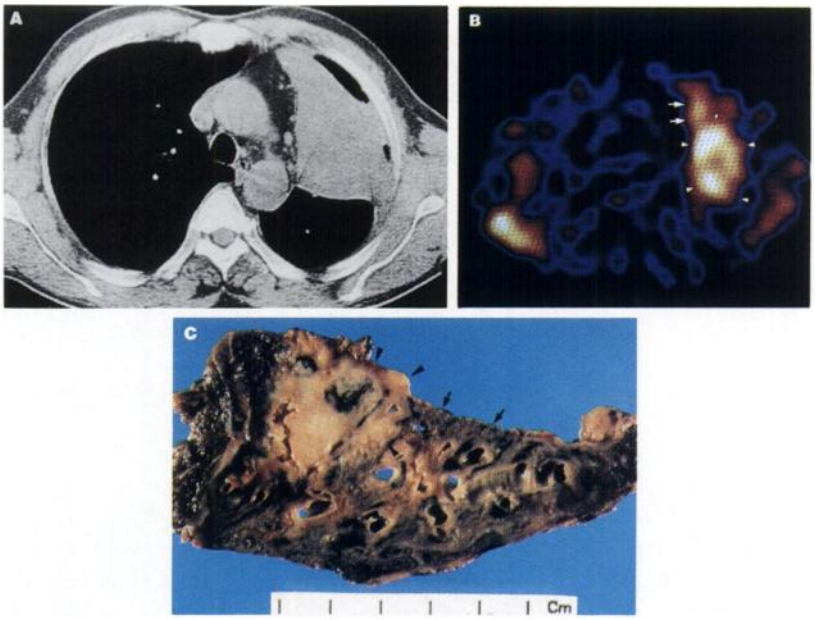

FIGURE 1. A 52-yr-old male patient with well differentiated carcinoma and distal endogenous lipoid pneumonia. (A) Precontrast-enhanced CT reveals collapse consolidation on left upper lobe. (B) SPECT shows increased uptake within the tumor with central photon defect (arrow heads). Increased radiotracer uptake is also seen within the atelectasis, anterior to the mass (arrows). (C) Gross pathologic specimen shows a central large tumor mass with necrosis (arrow heads) and collapse consolidation anterior to the mass (arrows).

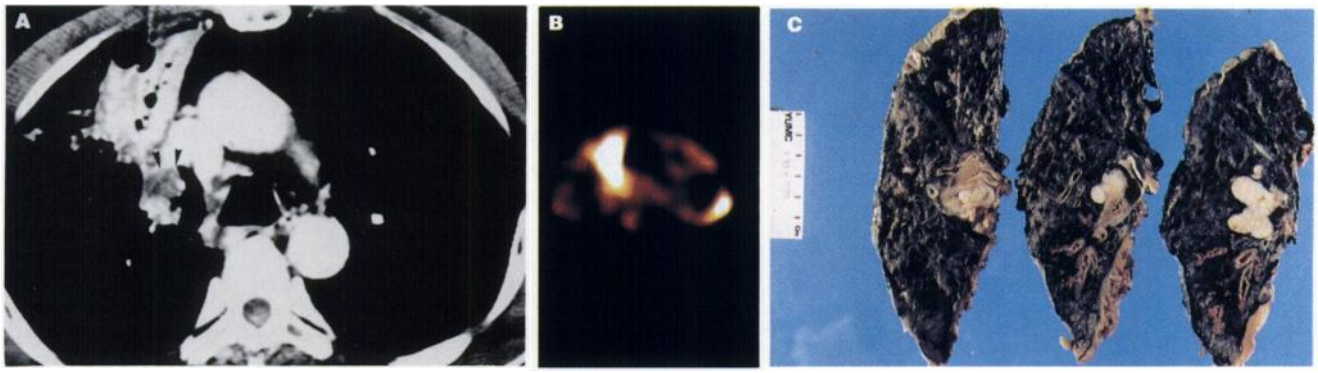

FIGURE 2. A 53-yr-old male patient with moderately differentiated carcinoma associated with bronchopneumonia in collapsed lung. (A) Contrast-enhanced chest CT shows a low-density central mass (arrow heads) with distal collapse. (B) SPECT reveals intense radiotracer uptake within both tumor and atelectasis. (C) Pathology clearly demonstrates round central mass.

RESULTS

Pathologic Findings

All patients had a central squamous carcinoma with distal collapse or consolidation. The tumor sizes ranged from 1.3 to 6 cm in diameter. Of the nine tumors, three were poorly differentiated, two were moderate, four were well differentiated and two had a central necrosis. The pathologic nature of collapse was obstructive pneumonia without superimposed inflammation in five and necrotizing bronchiolitis or abscess in four patients associated with bronchopneumonia.

SPECT Findings

In early SPECT images taken 1 hr after injection of ^{201}Tl, all of the tumor masses were visualized as Grade+++ in seven and Grade+ and Grade++ in one each. The smallest tumor was 1.3 cm in diameter. Necrotic areas were shown as photon deficient. However, collapsed lung also showed intense uptake as well; Grade++ in five and Grade+++ in four. The radioactivity within the tumor was higher in four

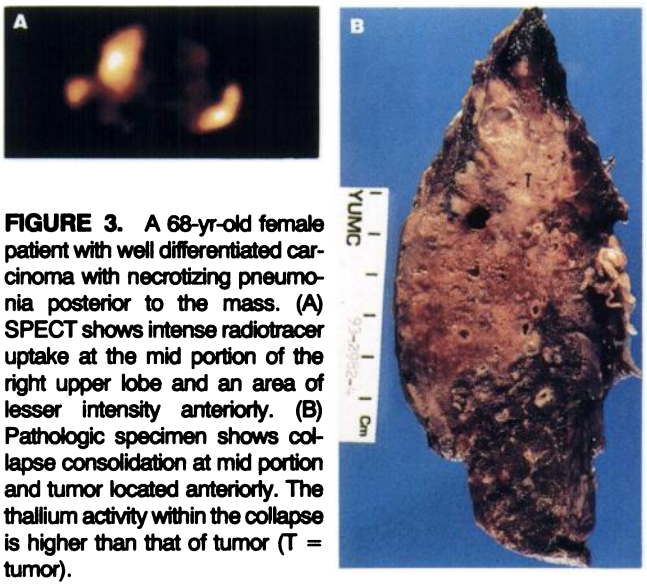

FIGURE 3. A 68-yr-old female patient with well differentiated carcinoma with necrotizing pneumonia posterior to the mass. (A) SPECT shows intense radiotracer uptake at the mid portion of the right upper lobe and an area of lesser intensity anteriorly. (B) Pathologic specimen shows collapse consolidation at mid portion and tumor located anteriorly. The thallium activity within the collapse is higher than that of tumor (T = tumor).

TABLE 1
Pathologic and SPECT Findings of Central Bronchogenic Cancer

Patient	Tumor size	Differentiation	Inflammation in collapse	Early SPECT	
				T	C
1	1.3 × 1.2	PD	None	+	++
2	3.0 × 2.0	PD	None	+++	+++
3	3.0 × 2.8	PD	None	+++	++
4	5.0 × 4.0	WD	None	+++	++
5	5.0 × 5.0	WD	None	+++	++
6	4.8 × 4.0	MD	Pneumonia with abscess	+++	++
7	6.0 × 6.0	WD	Pneumonia	++	+++
8	4.5 × 4.0	MD	Pneumonia	+++	+++
9	4.5 × 3.0	WD	Pneumonia	+++	+++

PD = poorly differentiated; MD = moderately differentiated; WD = well differentiated; T = tumor; and C = collapse.

(Fig. 1), equal in three (Fig. 2), and lower than atelectasis in two (Fig. 3). Although thallium activity within the atelectasis superimposed with inflammation tended to be slightly higher than that without inflammation, both lesions showed increased thallium uptake (Table 1). An area in the vicinity of pleural effusion also demonstrated increased thallium uptake despite the lack of pathologic evidence of pleural or chest wall invasion (Fig. 4).

On the delayed scan, thallium uptake within the atelectasis appeared less than that of the early SPECT image in two of five patients, while tumor activity showed sustained retention (Fig. 4).

DISCUSSION

Thallium-201, like potassium, has been used to evaluate tumor viability since it passes intracellularly to viable tumor. Recent investigations have demonstrated a potential role for ^{201}Tl scintigraphy in the evaluation of brain, lung, bone and soft tissue, breast, thyroid carcinomas and lymphoma (*6–11*).

The mechanisms of thallium uptake in tumor have been studied extensively, however, details have not been entirely elucidated. Various theories such as sodium-potassium ATPase activation (*12*), increased blood flow (*8*), Tl^+-Na^+2Cl^--cotransport system, as well as calcium ion channel exchange (*13*), tumor viability and increased cell membrane potential (*14*) are considered to be important factors.

On the basis of these tumor uptake mechanisms, efforts to detect intrathoracic malignancy have been attempted, although the foci of non-neoplastic lesions such as abscess (*15*), pulmonary actinomycosis (*16*), active sarcoidosis and tuberculosis (*7*) can also be seen as areas of increased

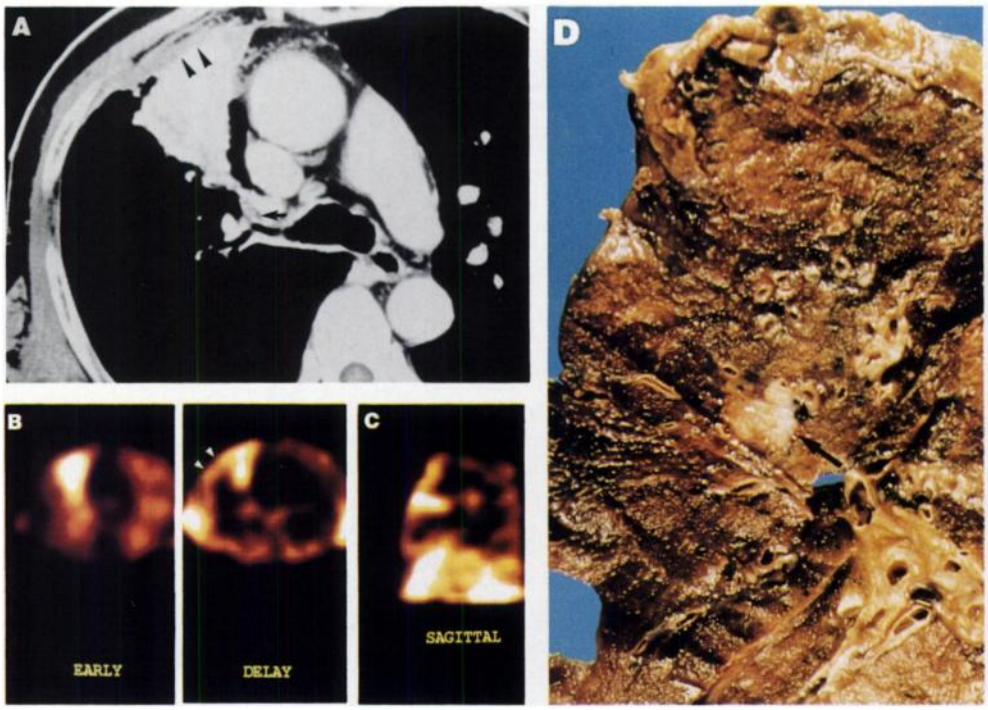

FIGURE 4. A 61-yr-old male patient with poorly differentiated carcinoma with localized atelectasis. (A) Contrast-enhanced CT shows collapse consolidation on anterior segment of right upper lobe and a small nodule at the orifice of anterior segmental bronchus (arrow). Small amount of pleural effusion is seen anteriorly (arrow heads). (B) SPECT shows increased uptake within the collapse, as well as the area in the vicinity of pleural effusion (arrow heads). The tumor is difficult to be distinguished from the surrounding lung parenchyme on the early scan. Delayed SPECT clearly demonstrates both tumor and atelectasis due to washout of normal lung activity. Delayed sagittal image (C) and pathologic lung section (D) show a small nodule, 1.3 cm in diameter centrally.

activity. Therefore, several investigations have been studied to differentiate a malignant tumor from non-neoplastic lesions.

Thallium in inflammatory or benign lesions decreased with time but prolonged retention of radioactivity with delayed washout was observed in malignant tumors (*9,11*), which indicates that delayed scans seem to be more valuable in the differentiation between benign and malignant lesions. On the contrary, our results demonstrated sustained retention of radioactivity within the atelectasis up to 4 hr in three out of five patients on a delayed scan. The exact mechanism of prolonged retention of radioactivity within the atelectasis is unknown. We assumed altered biodistribution of the ionic molecule may be one of the causative factors. Airless lung tissue peripheral to a totally occluded bronchus may produce pulmonary edema due to increased surface tension and disruption of the alveolar lining layers (*17*). The edema fluid secreted through the pulmonary vessels with abnormally increased permeability may not resorb but be phagocytosed by alveolar marcophages (*13*). Therefore, we assumed secreted thallium into the interstitial space of atelectatic lung was retained due to delayed lymphatic or venous drainage. The validity of this assumption could be determined by measuring the thallium activity in regard to the effect of atelectasis on pulmonary capillary permeability and lymphatic flow. In conclusion, our study illustrates the need for caution in the interpretation of thallium scintigraphy in patients with central bronchogenic carcinoma with distal atelectasis.

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