Assessment of Residual Tumor Viability in Thymic Carcinoma by Sequential Thallium-201 SPECT: Comparison with CT and Biopsy Findings

Hikaru Seto, Masanari Kageyama, Masashi Shimizu, Yi-wei Wu, Tetsuya Kamei and Masao Kakishita

Department of Radiology, Toyama Medical and Pharmaceutical University, Toyama City, Toyama, Japan

We present a case of ^{201}Tl accumulating thymic carcinoma, in which sequential CT scans demonstrated a steady decrease in tumor volume. The presence of a residual mass on CT scans after the completion of therapy presented the clinical dilemma of whether or not a viable tumor remained. Sequential ^{201}Tl SPECT images demonstrated a marked decrease in tumor uptake. At 2 wk after therapy, no significant accumulation of ^{201}Tl in the region of the residual mass was observed, indicating a lack of viable tumor. A biopsy specimen revealed no tumor cells. Sequential histopathologic findings were correlated well with the findings of ^{201}Tl SPECT rather than those of CT. Thallium-201 SPECT is of great clinical value in assessing tumor viability in the course of therapy.

Key Words: thallium-201; SPECT; viability; thymic carcinoma; computed tomography

J Nucl Med 1994; 35:1659–1661

Computed tomography (CT) has become a standard method to determine the extent of disease and to evaluate disease response to therapy in malignant tumors. However, the presence of a residual mass detected by CT after the completion of therapy always poses a clinical dilemma for the oncologist as to whether or not further therapy is to be undertaken (*1,2*). Gallium-67-citrate has been used to differentiate residual active tumor from fibrosis in lymphoma, and a negative gallium scan has been thought to exclude the presence of active tumor (*3,4*). Although ^{67}Ga-citrate still has its indications in the staging and follow-up of lymphoma (*5*), there are several limitations in tumor imaging. These include uptake by inflammatory lesions and thymic rebound, and slow blood clearance (*5–8*). In contrast, ^{201}Tl-chloride has several advantages in tumor imaging such as rapid blood clearance and better image quality as compared to ^{67}Ga-citrate. Therefore, ^{201}Tl-chloride has been used in a variety of malignant diseases including tumors of thyroid, lung, brain, bone and thymus (*9–16*). Recently, ^{201}Tl scintigraphy has also been used to monitor the treatment response of malignant tumors because of less uptake by healing bone and thymic rebound, and more accurate reflection of viable tumor burden than ^{67}Ga-citrate (*14,16–18*).

The purpose of this report is to describe the validation of sequential ^{201}Tl-SPECT for the assessment of residual tumor viability and to compare with concurrent CT scans and biopsy results in a patient with thymic carcinoma.

CASE REPORT

A 75-yr-old woman presented with pain and a mass on the anterior chest wall. A percutaneous biopsy was positive for poorly differentiated squamous cell carcinoma. Sequential ^{201}Tl studies were performed 10 min following the administration of 3.0 mCi of ^{201}Tl-chloride (Nihon Medi-physics, Japan). SPECT was performed using a three-detector gamma camera (Tohsiba 9300A) with a low-energy collimator with 20% windows centered over a 72-keV energy peak. A 360° SPECT of the chest was performed with an acquisition time of 30 sec/view for 64 steps. Contiguous 10-mm thick axial images were reconstructed. Simultaneously, CT was performed using a Toshiba 900S scanner at 10-mm intervals. Tumor volumes were obtained to measure the maximum tumor areas on the sequential CT scans. Tumor-to-lung radioactivity ratios were obtained to determine ROIs over the tumor and surrounding normal lung on sequential ^{201}Tl SPECT images. Biopsy examinations using a 21-gauge needle were performed under the guidance of CT at the same times.

Initial CT and ^{201}Tl SPECT demonstrated a large lobulated mass with intense radiotracer uptake between the sternum and aorta on the left side, invading the chest wall (Fig. 1A). The patient was treated with radiotherapy, including x-ray (60 Gy) and electron beam (10 Gy). Chemotherapy (carboplatin 100 mg) was also performed three times during this period. At the completion of therapy, 8 wk from diagnosis, follow-up CT and ^{201}Tl SPECT scans were obtained (Fig. 1B). There was a steady decrease in tumor volume with reduced radiotracer uptake. A marked reduction of tumor cells was also noted histologically. The third CT and ^{201}Tl SPECT were obtained at 10 wk from diagnosis (Fig. 1C). A small residual mass was still noted on the CT scan, however, no

Received Nov. 11, 1993; revision accepted Apr. 22, 1994.
For correspondence or reprints contact: Hikaru Seto, MD, Department of Radiology, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama City, Toyama, 930-01, Japan.

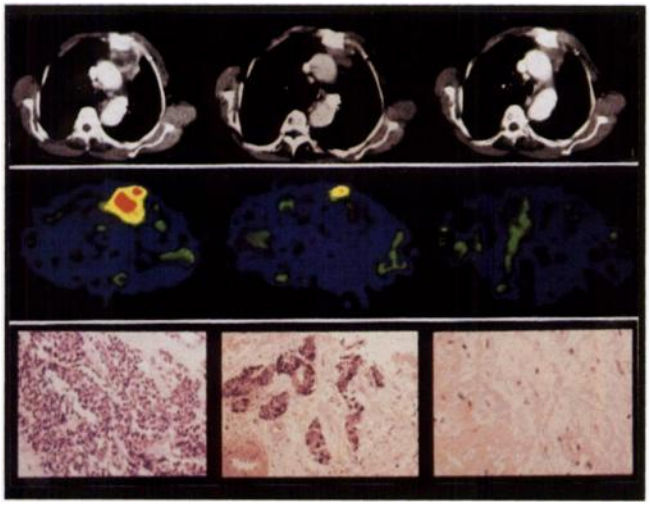

FIGURE 1. Sequential CT scans (upper panel), ^{201}Tl SPECT images (middle panel) and histopathologic results (lower panel) of a 75-yr-old female with thymic carcinoma: (A) Before therapy, (B) At the end of therapy, 8 wk from diagnosis and (C) 10 wk from diagnosis.

significant radiotracer uptake was noted in the region of the mass on the SPECT image. A faint linear uptake was observed along the medial portion of right lung, corresponding to the site of radiation pneumonitis on the CT scan. Biopsy of the mass revealed no tumor cells. Tumor volume measured by sequential CT was decreased from 37.6 to 23.1 to 21.8 cm^3. On the other hand, the tumor-to-lung ratio measured by sequential SPECT was dramatically decreased from 0.705 to 0.078 to 0.006 (Fig. 2).

DISCUSSION

A residual mass detected by CT after the completion of therapy may not indicate the presence of viable tumor (*1,2*). Therefore, it is essential to determine whether or not a viable tumor is still present. A biopsy is the only definitive test to confirm the presence of viable tumor. Ideally, a sampling of a large amount of tissue is required for accurate assessment of tumor viability. However such sequential samplings are difficult and sometimes very dangerous when a tumor is localized deeply. Fortunately, in our case, the tumor was localized in the anterior mediastinum, and biopsy specimens were successfully obtained three times under the guidance of CT. Recently, ^{67}Ga SPECT has been used to determine the presence of active tumor when a CT scan still shows a residual mass in lymphoma (*3,4*). Gallium-67-citrate, however, has several disadvantages such as uptake by inflammatory lesions, thymic rebound and slow blood clearance, (*6–8*). In contrast, ^{201}Tl-chloride has several advantages over ^{67}Ga-citrate because of rapid blood clearance, better image quality and less uptake by healing bone and thymic rebound (*16,18*). Thallium-201 uptake by tumor is dependent on sodium potassium ATPase pump activity, and therefore its uptake reflects the viability and metabolic activity of the tumor cells (*19–21*). In our case, ^{201}Tl uptake by the thymic carcinoma decreased as the therapy progressed. At 2 wk after the completion of therapy, a residual mass was still seen on the CT scan, however no significant ^{201}Tl accumulation in the mass was observed on the ^{201}Tl SPECT image. A biopsy revealed no tumor cells (Fig. 1C). A biopsy specimen may not always represent global changes of the tumor. In our patient, however, sequential biopsy findings were correlated well with the findings of ^{201}Tl SPECT rather than those of CT. Moreover, follow-up enhanced CT 1 mo later did not show any changes in the residual mass of the anterior mediastinum. Therefore, we considered that the mass was not viable because of the lack of ^{201}Tl uptake and absence of changes on the CT scan. Even though biopsy remains the only definitive test to examine tumor viability, it is often difficult to perform in the clinical setting. Sequential ^{201}Tl SPECT is a noninvasive method that provides useful information on tumor viability in the course of therapy.

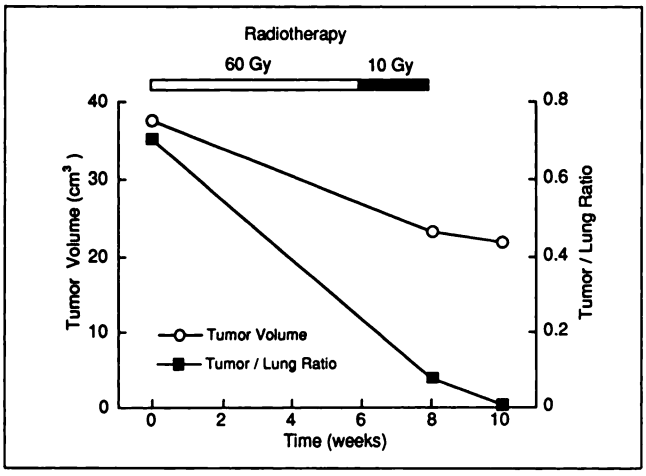

FIGURE 2. Changes in tumor volume and uptake ratio of ^{201}Tl assessed by sequential CT and SPECT in the course of therapy.

ACKNOWLEGMENTS

The authors thank Professor Kinichi Hisada, Kanazawa University School of Medicine for valuable discussion and the staff of the Nuclear Medicine Division for technical assistance.

REFERENCES

1. Lewis E, Bernardino ME, Salvador PG, et al. Post-therapy CT-detected mass in lymphoma patients: is it viable tissue? *J Comput Assist Tomogr* 1981;6:792–795.
2. Canellos GP. Residual mass may not be residual disease. *J Clin Oncol* 1988;6:931–933.
3. Tumeh SS, Rosenthal DS, Kaplan WD, et al. Lymphoma: evaluation with Ga-67 SPECT. *Radiology* 1987;164:111–114.
4. Kostakoglu L, Yeh SDJ, Portlock C, et al. Validation of gallium-67-citrate single-photon emission computed tomography in biopsy-confirmed residual Hodgkin's disease in the mediastinum. *J Nucl Med* 1992;33:345–350.
5. Front D, Bar-Shalom R, Epelbaum R, et al. Early detection of lymphoma recurrence with gallium-67 scintigraphy. *J Nucl Med* 1993;34:2101–2104.
6. Kramer EL, Sanger JJ, Garay SM, et al. Gallium-67 scans of the chest in patients with acquired immunodeficiency syndrome. *J Nucl Med* 1987;28: 1107–1114.
7. Holdstok G, Ligorria JE, Krawitt EL. Gallium-67 scanning in patients with Crohn's disease: an aid to the diagnosis of abdominal abscess. *Br J Surg* 1982;69:277–278.
8. Donahue DM, Leonard JC, Basmadjian GP, et al. Thymic gallium-67 localization in pediatric patients on chemotherapy: concise communication. *J Nucl Med* 1981;22:1043–1048.

9. Cox PH, Belfer AJ, Van der Pompe WB. Thallium-201-chloride uptake in tumours, a possible complication in heart scintigraphy. *Br J Radiol* 1976; 49:767–768.
10. Hisada K, Tonami N, Miyamae T, et al. Clinical application of tumor imaging with Tl-201-chloride. *Radiology* 1978;129:497–500.
11. Tonami N and Hisada K. Thallium-201 scintigraphy in postoperative detection of thyroid cancer. *Radiology* 1980;136:461–464.
12. Fukuda T, Itami M, Sawa H, et al. A case of thymona arising from undescended thymus. *Eur J Nucl Med* 1980;5:465–468.
13. Hoefnagel CA, Delprat CC, Marcuse HR, et al. Role of thallium-201 total-body scintigraphy in follow-up of thyroid carcinoma. *J Nucl Med* 1986;27: 1854–1857.
14. Kaplan WD, Takvorian T, Morris JH, et al. Thallium-201 brain tumor imaging: a comparative study with pathologic correlation. *J Nucl Med* 1987;28:47–52.
15. Tonami N, Shuke N, Yokoyama K, et al. Thallium-201 single photon emission computed tomography in the detection of suspected lung cancer. *J Nucl Med* 1989;30:997–1004.
16. Ramanna L, Waxman A, Binney G, et al. Thallium-201 scintigraphy in bone sarcoma: comparison with gallium-67 and technetium MDP in the evaluation of chemotherapeutic response. *J Nucl Med* 1990;31:567–572.
17. Yoshii Y, Satou M, Yamamoto T, et al. The role of thallium-201 SPECT in the investigation and characterization of brain tumors in man and their response to treatment. *Eur J Nucl Med* 1993;20:39–45.
18. Harris EW, Rakow JI, Wener M, et al. Thallium-201 scintigraphy for assessment of a gallium-67 avid mediastinal mass following therapy for Hodgkin's disease. *J Nucl Med* 1993;34:1326–1330.
19. Gehring PF, Hammond PB. The interrelationship between thallium and potassium in animals. *J Pharm Exp Ther* 1967;55:187–201.
20. Ando A, Ando I, Katayama M, et al. Biodistribution of ^{201}Tl in tumor bearing animals and inflammatory lesions induced in animals. *Eur J Nucl Med* 1987;12:567–572.
21. Sehweil AM, McKillop JH, Milroy R, et al. Mechanism of ^{201}Tl uptake in tumors. *Eur J Nucl Med* 1989;15:376–379.