Folllw-up Study of Postoperative Patients with Thyroid Cancer by Thallium-201 Scintigraphy and Serum Thyroglobulin Measurement

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The utility of ^{201}Tl scintigraphy and thyroglobulin measurement in the follow-up observation of postoperative patients with thyroid cancer was evaluated. Thallium-201 scintigraphy was performed in 149 postoperative patients with thyroid cancer. Serum thyroglobulin concentration was concomitantly evaluated in 86 patients. Among 55 patients with positive ^{201}Tl scans, 51 patients (92.7%) had recurrent diseases, while 80 of 94 patients (85.1%) with negative scans were free of disease. Twenty-five of 28 patients (89.3%) with elevated thyroglobulin levels were recurrent and 43 of 58 patients (74.1%) with normal thyroglobulin level had no recurrence nor metastasis. All 19 patients with positive ^{201}Tl scans and elevated thyroglobulin level had recurrent lesions. Seven of 10 patients with negative ^{201}Tl scans and elevated thyroglobulin level showed the presence of metastasis. By concomitant measurement of serum thyroglobulin, more than half of the recurrent patients with negative ^{201}Tl scintigraphy were detected. Both ^{201}Tl scintigraphy and serum thyroglobulin measurement should be undertaken in the follow-up evaluation of postoperative patients with thyroid cancer.

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Since the application of ^{201}Tl-chloride for thyroid tumor imaging, several authors reported the usefulness of ^{201}Tl in diagnosing thyroid malignant nodules (*1,2*). The accumulation of ^{201}Tl was also detected in metastatic or recurrent lesions in patients with thyroid cancer (*3*). Although the use of ^{201}Tl imaging for detection of recurrent or metastatic lesions in postoperative patients is still limited, it has generated considerable interest (*4,5*).

The measurement of serum thyroglobulin (Tg) levels has also become an important part of the diagnosis and management of patients with thyroid cancer (*6*). It has been suggested that the measurement of serum Tg could provide a sensitive marker for the presence of metastases and/or recurrent lesions in the patients with thyroid cancer who underwent thyroidectomy (*7–9*).

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The purpose of this study was to evaluate the significance of ^{201}Tl scintigraphy and Tg measurement in the follow-up of postoperative patients with thyroid cancer.

MATERIALS AND METHODS

These studies were carried out in 149 postoperative patients with thyroid cancer (31 males and 118 females), aged 15–81 yr (mean age, 51.6 yr). There were 117 patients with papillary adenocarcinoma, 27 cases of follicular adenocarcinoma, 2 cases of undifferentiated carcinoma, 2 cases of malignant lymphoma, and one case of medullary carcinoma. The patients had undergone total thyroidectomy (48 cases), hemithyroidectomy (93 cases), or subtotal thyroidectomy (8 cases). The period after thyroidectomy ranged from 1 mo to 30 yr (mean, 4.9 yr).

Thallium-201 scintigraphy was performed between September 1981 and April 1986. Eighty-four patients who were followed for more than 3 yr after ^{201}Tl scintigraphy without appearance of metastatic or recurrent lesions were considered to be free of disease. All 66 patients who were judged to have suffered recurrence were histologically confirmed by operation or biopsy.

Thallium-201 (74 MBq) was given intravenously and imaging of the anterior neck and chest was performed 10 min later using a gamma camera (Gamma View-F RC-IC-1635LF, Hitachi Medical Cooperation, Chiba, Japan) equipped with a high-resolution parallel-hole collimator. Preset information density was 0.5K counts/cm^2 or the preset time was 300 sec for patients who had total thyroidectomies. The collimator-to-patient distance was 6 cm. Energy selection was set at 68-84 keV.

Blood samples for serum Tg measurement were drawn from the patients with differentiated thyroid carcinoma at the time of ^{201}Tl scintigraphy. Serum Tg was determined by a double antibody radioimmunoassay using a commercially available kit (Eiken Immunochemical Laboratory, Tokyo, Japan). Normal range calculated from 30 normal subjects was 0-30 ng/ml. Since the anti-Tg antibody may cause false results in the assay, all sera with positive anti-Tg (>10%) were excluded from evaluation. Serum Tg concentration could be evaluated in 86 patients.

Data were analyzed for statistical significance by chi-square test.

RESULTS

The ^{201}Tl scintigraphic results are shown in Table 1. Fifty-five patients had positive scans and 94 patients had negative scans. Of 55 patients with positive scans, 51 patients (92.7%) were revealed to have recurrent lesions,

TABLE 1
Thallium-201 Scintigraphy and Outcome

			Recurrence	No recurrence
^{201}Tl	positive	55 cases	51 (40)	4 (1)
	negative	94 cases	14 (6)	80 (14)

Numbers in parentheses are the patients suspected of having lesions at the time of ^{201}Tl scintigraphy.

True-positive 78.5%, false-negative 21.5%, false-positive 4.8%, true-negative 95.2%, and accuracy 86.9%.

but 4 patients (7.3%) had no signs of recurrence for 3–9 yr. In 11 of 51 recurrent patients with positive ^{201}Tl scans, no recurrent lesions were suspected at the time of ^{201}Tl scintigraphy, but metastatic neck lymph nodes in 8 cases and neck recurrent mass in 3 cases appeared within 3 yr. A representative case from these 11 patients is shown in Figure 1.

Among the 94 patients with negative ^{201}Tl scans, 14 patients (14.9%) were recurrent and 80 patients (85.1%) had no evidence of recurrence for more than 3 yr. In 6 of the 14 patients with negative ^{201}Tl scans who subsequently developed recurrent disease, additional ^{201}Tl scintiscans were positive at the time that the metastatic or recurrent lesions were physically apparent. An example is shown in Figure 2. Neck mass in 14 patients without ^{201}Tl accumulation who had no evidence of recurrence was confirmed to be lymphadenitis in 9 cases, inflammatory tissue around ligation in 4 cases, and thyroid cyst in 1 case.

As shown in Table 2, 26 of 29 patients (89.7%), whose serum Tg levels were more than 30 ng/ml, were diagnosed with recurrent lesions, and 43 of 57 patients (75.4%), whose serum Tg levels were less than 30 ng/ml, had no evidence of recurrent lesions for more than 3 yr.

Serum Tg levels were compared with the results of ^{201}Tl scintigraphy in Figure 3. The results of ^{201}Tl were significantly correlated with the level of serum thyroglobulin ($p<0.001$). Among 30 patients with positive ^{201}Tl scans, Tg concentration was more than 30 ng/ml in 19 patients

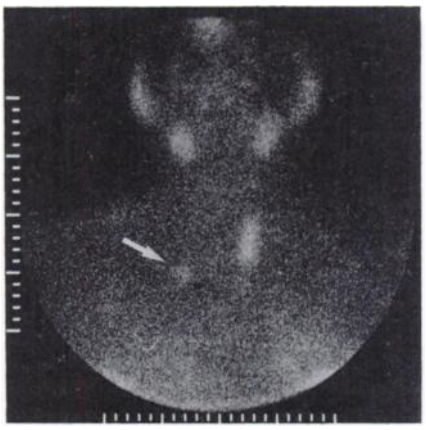

FIGURE 1. A 54-yr-old man had right hemithyroidectomy due to papillary adenocarcinoma in August 1983. Thallium-201 scintigraphy in May 1984 showed right supraclavicular accumulation but no neck mass was palpated. After 2 yr, a right supraclavicular nodule was noticed which was surgically proven to be a metastatic lymph node.

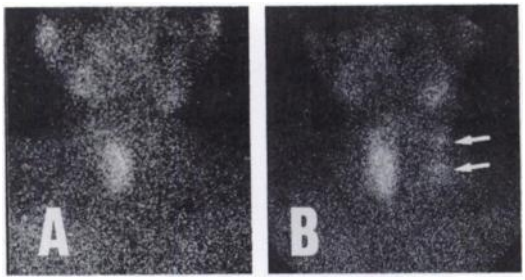

FIGURE 2. A 61-yr-old woman had left hemithyroidectomy due to papillary adenocarcinoma in January 1984. Thallium-201 scintigraphy in April 1985 (A) showed no abnormal accumulation. Thallium-201 scintigraphy in September 1986 (B) showed accumulation in left lateral cervical lymph nodes which were surgically proven to be metastatic lesions.

(63.3%), all of whom were diagnosed with recurrent lesions. Serum Tg levels were less than 30 ng/ml in 11 patients (36.7%). Three of them had no evidence of recurrence. Among the 56 patients without abnormal ^{201}Tl accumulation, 10 patients (17.9%) showed Tg concentration of more than 30 ng/ml. Seven of these 10 patients (70%) had evidence of recurrence. Serum Tg levels were less than 30 ng/ml in 46 patients, and 40 of these 46 patients (87.0%) had no evidence of recurrence.

DISCUSSION

In this study, ^{201}Tl scintigraphy and serum Tg measurements were evaluated to detect recurrent or metastatic lesions in postoperative patients with thyroid cancer. Since ^{201}Tl imaging was performed in the neck and chest, ^{201}Tl scintigraphy disclosed only local recurrence or metastasis in this study.

Iodine-131 scintigraphy had been the most widely used method to detect recurrent or metastatic lesions in postoperative patients with thyroid cancer. However, ^{131}I scintigraphy has many disadvantages, such as the need of ablation of normal thyroid tissue, restriction of dietary iodine intake and discontinuation of thyroid hormone medication. On the contrary, ^{201}Tl can be performed without such preparation. Thallium-201 scintigraphy was reported in metastatic deposits postoperatively in 7 of 15 patients with well-differentiated thyroid cancer. There was tumor concentration of radioiodine in only three patients (*4*). In our study, 78.5% of recurrent cases could be

TABLE 2
Thyroglobulin and Outcome

			Recurrence	No recurrence
Tg	>30 ng/ml	29 cases	26 (15)	3 (0)
	<30 ng/ml	57 cases	14 (10)	43 (9)

Numbers in parentheses are patients who had suspected lesions at the time of ^{201}Tl scintigraphy.

True-positive 65.0%, false-negative 35.0%, false-positive 6.5%, true-negative 93.5%, and accuracy 79.3%.

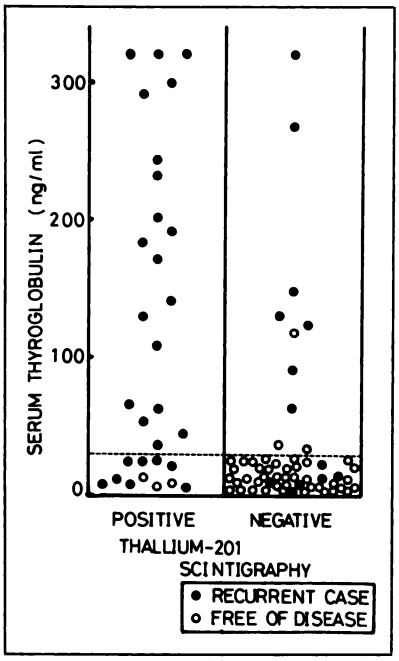

FIGURE 3. Thallium-201 scintigraphy and serum thyroglobulin concentration in postoperative patients with thyroid cancer.

detected by ^{201}Tl. Reimaging with ^{201}Tl in 6 of 14 patients with negative ^{201}Tl scans who were subsequently diagnosed with recurrent or metastatic lesions were positive at the time that the metastatic or recurrent lesions were evident. These false-negative results might be due to either the limited resolution of the gamma camera or insufficient accumulation of ^{201}Tl.

Although Tg determination is of limited value in the diagnosis of untreated patients with thyroid tumor, this measurement is useful in monitoring patients who underwent removal of differentiated thyroid tumor (*6–9*). In our study, 26 of 40 recurrent cases (65%) showed elevated levels of Tg. This value was rather lower than those reported by others (*7,8,10,11*). This might be due to the difference of the timing of blood sampling. We measured Tg concentration at the time of ^{201}Tl scintigraphy and compared the value with the later outcome in the following 3 yr. The metastatic or recurrent lesions might not be sizable enough to release substantial amount of Tg at the time of Tg measurement. It is well-known that the increase in the thyrotropin level results in the elevation of Tg level (*7–9,11*). In this study, we measured Tg concentration without discontinuation of thyroid medication. This might be the other reason of lower positivity of Tg level in the patients with recurrent lesions.

Serum Tg concentrations increased only in differentiated thyroid cancer, whereas ^{201}Tl was reported to accumulate in undifferentiated cancer, malignant lymphoma and medullary carcinoma as well as differentiated carcinoma (*2,12*). In this study, we observed ^{201}Tl accumulation in one of two patients with undifferentiated carcinoma who were recurrent. In the patients with malignant lymphoma and medullary carcinoma, no accumulation of ^{201}Tl was demonstrated because of no recurrence nor metastasis. The neck lymph node metastasis, which was too small to increase serum Tg level substantially, could be easily detected in ^{201}Tl scintigraphy (*11*). Serum Tg determination could disclose the distant metastatic lesions, although ^{201}Tl scintigraphy could detect the recurrent or metastatic lesions only in neck and chest of which imagings were undertaken. In our study, there were three patients with metastatic bone lesions, and all of them showed positive accumulation of ^{201}Tl in the cervical vertebra or ribs as well as elevation of Tg concentration.

Thallium-201 scintigraphy had an accuracy of 86.9% and serum Tg measurement had an accuracy of 79.3%. For detection of metastatic or recurrent lesions, ^{201}Tl scintigraphy was significantly more accurate than Tg measurement ($p<0.05$). However, ^{201}Tl could not detect all recurrent or metastatic cases. By concomitant measurement of serum Tg levels at the time of ^{201}Tl scintigraphy, more than half of the metastatic or recurrent tumors in patients with negative ^{201}Tl scintigraphy could be detected.

We believe that both ^{201}Tl scintigraphy and serum Tg measurement should be undertaken in the routine follow-up evaluation of postoperative patients with thyroid cancer.

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