

Thyroid carcinoma in solitary hot thyroid lesions on Tc-99m sodium pertechnetate scans

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Sixteen patients with nonsuppressible solitary hot thyroid lesions (SHTL) identified on T₃ suppression images using Tc-99m sodium pertechnetate were studied over a period of 5 years. Of the 16 patients, 7 (44%) had papillary adenocarcinoma (PAC) and 9 (56%) had follicular adenoma (FA). Of the 7 patients with PAC, 3 were toxic and 4 nontoxic. Of the 9 patients with FA, 2 were toxic and 7 nontoxic. The Tl-201 chloride thyroid scans were useful in locating SHTL and revealing extranodular thyroid tissue. The echography was sensitive to visualization of the nodule structures. However, there were no significant differences between the clinical findings, radionuclide images, and echograms between for PAC and FA. All patients with PAC were treated by partial thyroidectomy and there were neither regional nor distant metastasis in any of them. In conclusion, our study provided the following extremely interesting result: SHTL in the present series have a higher incidence of malignancy than previously reported autonomously functioning thyroid lesions (AFTL). Histological examination is necessary for the diagnosis and management of SHTL and surgical treatment should be considered.

Key words: Solitary hot thyroid lesions, Tc-99m sodium pertechnetate, Papillary adenocarcinoma, Histological examination

INTRODUCTION

THYROID SCINTIGRAPHY is an excellent method of evaluating regional functions of thyroid tissue. We¹ have routinely undertaken thyroid scans with Tc-99m sodium pertechnetate (Tc-99m) and Tl-201 chloride (Tl-201) for the evaluation of thyroid nodules.

From 1981 to 1987 we performed 3486 Tc-99m thyroid scans and found 22 patients with hot or warm nodules. Sixteen patients (0.46%) had undergone histologically examination of their solitary hot thyroid lesions (SHTL) which were nonsuppressible according to T₃ suppression images. For the diagnosis and management of these patients with SHTL, we performed scintigraphic and echographic evaluations and analyses of clinical and pathological findings.

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The following is a detailed report of our surprising results: the incidence of carcinoma (44%) in hot nodules was considerably higher than reported in previous studies²⁻¹¹ on AFTL or hot nodules on radioiodine scans.

MATERIALS AND METHODS

Twenty two patients had hot or warm nodules corresponding to palpable nodules on Tc-99m thyroid scans. One of them had toxic multinodular goiter and the other 21 patients had single nodules. For the 16 patients with solitary nodules, we performed clinical evaluations with radionuclide thyroid scans, ultrasonography (US) and blood chemistry, and histological examination of nodules.

Tc-99m thyroid uptake and images with Tc-99m or Tl-201 were obtained with an Ohio Nuclear Sigma 410 gamma camera equipped with a converging collimator. Thyroid scan and uptake were performed 30 minutes after an intravenous administration of 2 mCi of Tc-99m sodium pertechnetate (Tc-99m) as

Table 1 Clinical data for 16 patients with SHTL

Patient	Age	Sex	Nodule diameter (cm)	Histology of nodule	T ₃ ¶(90–170 (ng/ml)	T ₄ (5–14 µg/dl)	TSH (0.48–4.20 (µU/ml)	Thyroid state	TRAb	Tg (<30 ng/ml)
1	69	F	3.0	FA	198	10.7	u.d.	hyperthyroid	(–)	93
2	47	F	1.5	FA	185	16.3	0.22	hyperthyroid	(–)	26
3	43	F	2.0	FA	100	5.8	0.73	euthyroid	(–)	149
4	57	F	1.5	FA	140	9.1	2.10	euthyroid	(–)	48
5	58	F	4.5	FA	120	12.3	0.76	euthyroid	(–)	320<
6	60	F	3.6	FA	113	8.1	1.93	euthyroid	(–)	105
7	40	F	2.5	FA	108	7.0	0.69	euthyroid	(–)	148
8	54	F	0.5	FA	140	7.7	1.52	euthyroid	(–)	/
9	30	F	3.0	FA	126	9.0	1.53	euthyroid	(–)	87
10	72	M	2.8	PAC	224	20.5	u.d.	hyperthyroid	(–)	85
11	52	M	5.0	PAC	200	13.0	u.d.	hyperthyroid	(–)	320<
12	55	F	1.6	PAC	170	7.0	0.29	hyperthyroid	(–)	145
13	65	F	4.3	PAC	140	7.4	0.96	euthyroid	(–)	320<
14	37	F	2.5	PAC	140	9.9	0.55	euthyroid	(–)	202
15	39	F	3.5	PAC	91	6.3	1.68	euthyroid	(–)	173
16	38	F	4.5	PAC	99	4.7	1.56	euthyroid	(–)	227

FA: Follicular adenoma, PAC: Papillary adenocarcinoma, u.d.: Undetectable, ¶ Normal range.

previously reported.¹² Briefly, patients were laid in a supine position. A gamma camera was set at 10 cm from the anterior surface of the neck. The counts were accumulated in DEC PDP 11/34 for 2 minutes and the uptake rate was calculated by the previously described formula.¹² Tc-99m thyroid uptake in normal subjects was determined to be in the range of 0.4–2.5%. The suppression images and uptake rates were obtained after administration of L-T₃ (75 µg a day for 7 days). In cases in which the uptake was reduced to less than 50 percent of the initial value and less than 1% after T₃, the suppression test results were interpreted as positive. TI-201 chloride (TI-201) imaging was performed 20 minutes after an intravenous administration of 2 mCi of the tracer.

The US was performed with a high resolution realtime linear scanner, Yokogawa RT 2800, with a 7.5 megahertz transducer.

Serum thyroid hormones and TSH were measured with commercially available radioassay kits. Serum thyroglobulin (Tg) was measured with a doubleantibody RIA kit (Eiken Co. Tokyo). As positive Anti-Tg autoantibodies cause incorrect assay results in the Tg assay, anti-Tg antibodies were determined initially and antibody-positive serum was rejected for measurement of Tg. The TSH receptor antibody (TRAb) was measured with a TRAb kit (R.S.R. Ltd., U.K.).

Histological diagnosis of the nodules was based on microscopic findings for the tissue obtained by needle biopsy using a Vim-Silverman needle or operation.

In the present study a hyperactive focal area with

complete suppression of extranodular tissue was depicted as a “hot” nodule and a “warm” nodule indicated a relatively more hyperactive area with persistent extra nodular thyroid tissue activity.

The patients were diagnosed as toxic or nontoxic on the basis of the usual clinical and laboratory criteria for hyperthyroidism. In some cases, a TRH test was performed to determine the thyroid status.

RESULTS

Clinical data for 16 patients with SHTL are shown in Table 1. Of the 16 patients, 9 had follicular adenoma (FA) and 7 had papillary adenocarcinoma (PAC).

All 9 patients with FA were female whose average age was 51 years. The size of the nodules ranged from 0.5 cm to 4.5 cm, with an average of 2.5 cm in diameter. Of the 7 patients with PAC, 5 were female and 2 were male. Their mean age was 51 years. The size of the nodules ranged from 1.6 cm to 5.0 cm with a mean of 3.5 cm.

Two patients with FA and 3 with PAC showed mild hyperthyroidism. None of the hyperthyroid patients showed TSH response to TRH. TRAb was not detected in any of the 16 patients. Serum Tg concentrations were increased in 14 of 15 patients.

None of the 16 patients had either exophthalmos or cardiac complications.

The results of thyroid uptake and T₃ suppression tests with Tc-99m and the radionuclide scintigraphy and echography findings are shown in Table 2. The thyroid uptake in patients with FA ranged from 0.2

Table 2 The results of thyroid uptake and T₃ suppression tests with Tc-99m scintigraphy and echography findings

Patient	Thyroid uptake (0.4-2.5%)†	T ₃ suppression test	Scintigraphic findings of nodule		US
			Tc-99m	TI-201	
1	0.3	(-)	hot*	(+)†	solid-cystic
2	0.7	(-)	hot	(+)	solid
3	0.3	(-)	hot	normal	solid-cystic
4	0.2	(+)§	hot	(+)	solid
5	7.9	(-)	warm**	(+)	solid-cystic
6	2.4	(-)	warm	(+)	solid-cystic
7	3.0	(-)	warm	(+)	solid
8	0.3	(+)	warm	normal	solid-cystic
9	1.8	(-)	warm	(+)	solid-cystic
10	1.0	(-)	hot	(+)	solid
11	7.5	(-)	hot	(+)	solid
12	0.6	(+)	hot	(+)	solid-cystic
13	5.6	(-)	hot	(+)	solid-cystic
14	1.4	(-)	warm	normal	solid
15	0.4	(+)	warm	(-)‡	solid-cystic
16	1.8	(+)	warm	(+)	solid

†Normal range

§Suppression test was interpreted as positive if the uptake after administration of T₃ (75 µg/day for 7 days) was less than 50% of initial value and less than 1.0%

*All uptake in nodule; rest of gland suppressed, **Uptake in nodule more than in extranodular thyroid tissue

†Intense accumulation in nodule, ‡No uptake in nodule.

to 7.9% (mean±SD: 1.9±2.5%) and from 0.4 to 7.5% (mean±SD: 2.6±2.8%) for patients with PAC. The mean thyroid uptake was 2.0% in toxic patients and 2.3% in nontoxic patients.

Out of 9 FA patients, 7 tested negatively for T₃ suppression while 4 of the 7 PAC patients had negative suppression test results.

In all 16 patients warm or hot nodules were revealed on Tc-99m thyroid scans. The I-123 thyroid scans were also performed on 3 patients (Pt. 6, 9, 16). These images showed warm lesions similar to those on the Tc-99m scans.

Twelve patients showed focal accumulation of TI-201 corresponding to a hot or warm nodule on a Tc-99m scan. One patient (Pt. 15) showed a large defect on the TI-201 image that was identified by US as being a large cyst.

The US revealed that 9 out of 16 nodules developed into a cystic formation.

Of 9 patients with FA, 3 underwent surgical removal of the nodule, while the remaining 6 patients continued to be under observation. All patients with PAC were treated by partial thyroidectomy and neither regional nor distant metastases were detected in the PAC patients. All 5 toxic patients became euthyroid after undergoing partial thyroidectomies.

Serum Tg was measured about one month after the partial thyroidectomies performed on the 7 patients with PAC and 1 patient with FA. A marked

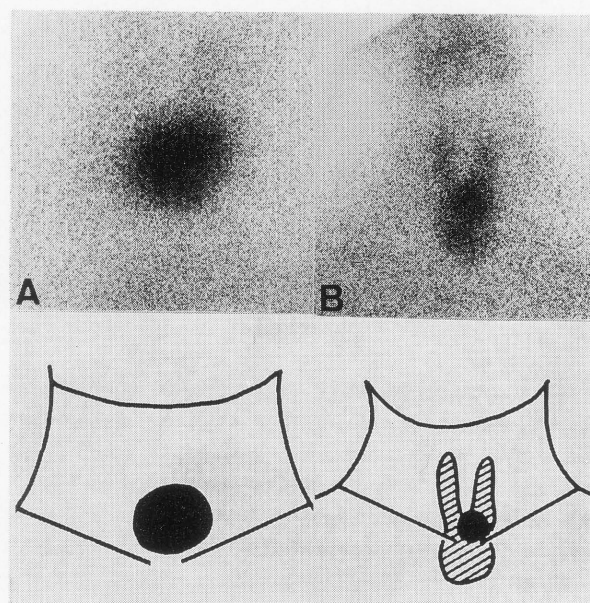


Fig. 1 (Patient 1), A: The Tc-99m thyroid scan shows a hot nodule with suppression of the remaining thyroid tissue. B: The TI-201 thyroid scan shows an intense accumulation of the tracer in the isthmus corresponding to a hot nodule on the Tc-99m scan and reveals both lobes and the substernal extending tumor.

reduction of serum Tg was observed in all cases.

The various cases are shown in Figs. 1-4.

Figure 1 shows Tc-99m and TI-201 images in a FA

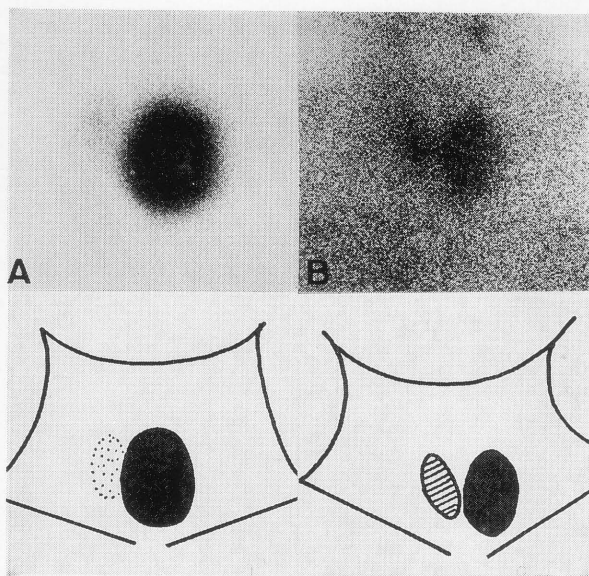


Fig. 2 (Patient 13) A: The Tc-99m thyroid scan shows a large hot nodule of the left lobe with almost complete suppression of the right lobe. B: The Tl-201 thyroid scan indicates an increase in radioactivity in the left lobe, permitting a view of the smaller right lobe.

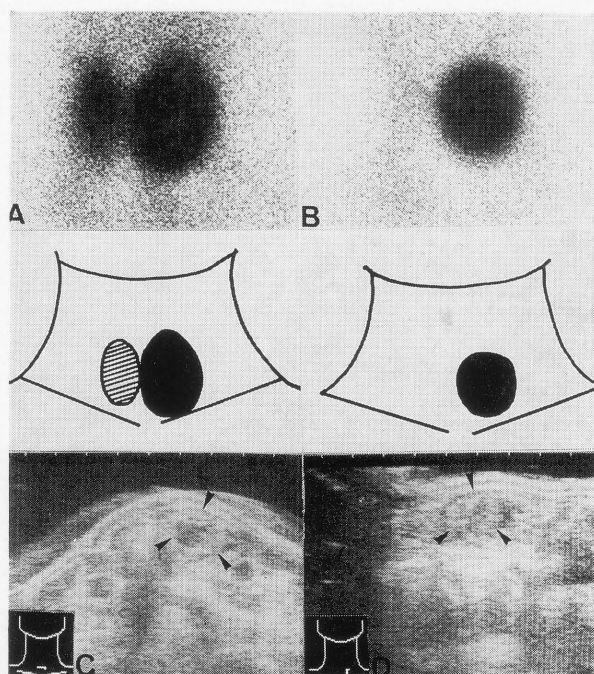


Fig. 3 (Patient 6) The T_3 suppression scan with Tc-99m. A: Thyroid scan before T_3 shows a warm nodule in the left lobe. B: The scan after T_3 shows a hot nodule in the left lobe, with complete suppression of the right lobe. Ultrasonogram. C: Transverse, D: Sagittal. Ultrasonograms demonstrate a well defined nodule with a cyst.

patient (patient 1). The Tl-201 scan demonstrated not only an abnormal accumulation of the tracer corresponding to the hot nodule on the Tc-99m scan,

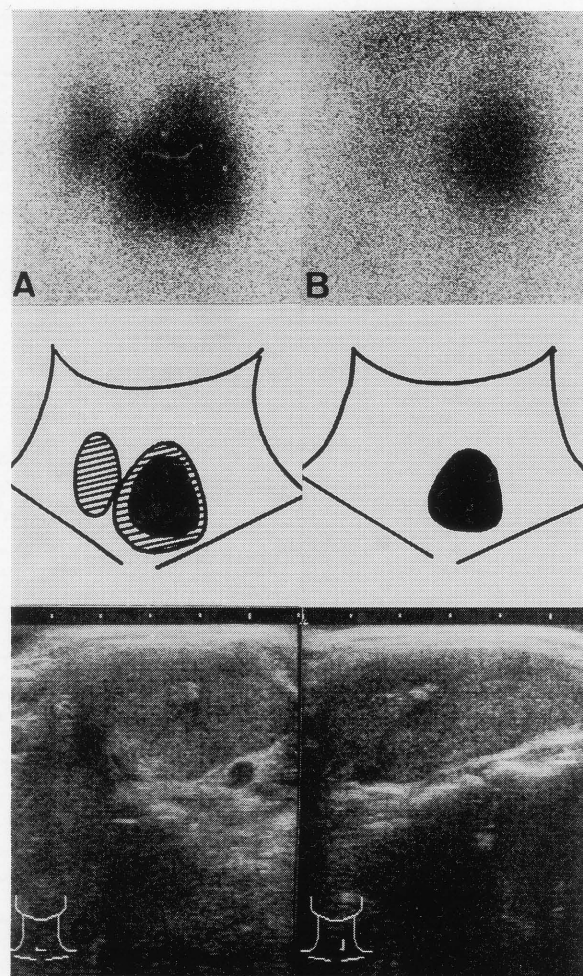


Fig. 4 (Patient 16) The T_3 suppression scan with Tc-99m. A: Thyroid scan before T_3 shows a large warm nodule in the left lobe. B: The scan after T_3 shows a remaining hot nodule in the left lobe, with almost complete suppression of the right lobe. Ultrasonogram. C: Transverse, D: Sagittal. Ultrasonograms show a large solid nodule.

but also a substernal extending tumor and both normal lobes that were nonvisualized on the Tc-99m scan. Surgical removal of the tumors was performed. There was no histological difference between the hot nodule and the substernal extending tumor.

Figure 2 shows Tc-99m and Tl-201 images in a PAC patient (patient 13). The Tc-99m scan shows a large hot left nodule with nonvisualization of the right lobe. The Tl-201 scan shows increased radioactivity in the left lobe and visualizes a small right lobe.

Figure 3 shows Tc-99m thyroid images before and after T_3 administration and ultrasonogram in a FA patient (patient 6). The warm left nodule was not suppressed after T_3 . Ultrasonograms indicate a nodule with a cyst.

Figure 4 shows also T_3 suppression images in a

PAC patient (patient 16). The warm left nodule is not suppressed by T_3 . The ultrasonogram shows a large solid nodule.

DISCUSSION

The thyroid imaging with Tc-99m is considered to be simple, easily performed, and a useful routine diagnostic tool for the evaluation of the regional functions of thyroid nodules. It has been reported that hot nodules are almost always benign and that malignant AFTL are exceedingly uncommon. The most interesting piece of evidence in the present study is that the incidence of carcinoma in SHTL was considerably higher at 7/16 (44%) than in previous reports²⁻¹¹ concerning carcinoma in AFTL.

From discrepancies between Tc-99m and radioiodine images which have been reported,¹³⁻¹⁶ one can see that the SHTL in the present study are not identical to AFTL which were confirmed by radioiodine scan. Although we did not have an opportunity to perform radioiodine scans on all of the carcinoma patients, three cases that also had warm lesions on radioiodine scans and five toxic cases that became euthyroid after surgical removal of the nodules were considered to be AFTL. That is, 4 of 7 PAC patients were considered to have AFTL. We don't know the exact reason for the high incidence of carcinoma in our small series studied by Tc-99m scans. An earlier article¹⁵ reported that the sensitivity of Tc-99m in detecting lesions was higher than that of I-123 scanning, and in the majority of cases the discrepancy was due to the fact that hot or warm lesions shown on the Tc-99m scan were cold or nonvisualized on the I-123 scan. Our study suggests that more hot lesions in carcinoma were detected on Tc-99m scans than on I-123 scans.

Another interesting finding is that neither regional nor distant metastases were found in the 7 carcinomas. It is conceivable that the cancer in SHTL in our study grows slowly. These thyroid tumors are considered to have the capacity to trap Tc-99m pertechnetate, independent of pituitary stimulation. The T_3 suppression image is useful in differentiating the tumors from TSH depending hyperplastic nodules.

Although the Tc-99m uptake of the nodules was not suppressed, some of those tested positively for T_3 suppression. As a significantly decreased uptake in extranodular tissue after T_3 in a small warm nodule might result in positive T_3 suppression, it is useful to compare the Tc-99m uptake of nodules before and after T_3 when evaluating the function of the nodules.

Since Tl-201 images are also very useful in visualizing both the tumor itself and the remaining thyroid tissue, TSH stimulation is not always necessary to confirm TSH dependent thyroid tissue. In case 1, a

Tl-201 image visualized both hot and nonvisualized tumor lesions on the Tc-99m scan.

It is certain that the US is a very important procedure for examination of the structure of a nodule but we could not differentiate carcinoma from benign tumors with a scan, US or any other clinical findings; therefore, it is very important to perform a histological examination.

Our results indicate that histological or cellular examination by needle or fine needle aspiration biopsy together with Tc-99m and Tl-201 scans is necessary for the diagnosis and management of SHTL.

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