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Evaluation of Thyroid Bed Nodules on Ultrasonography after Total Thyroidectomy: Risk for Loco-Regional Recurrence of Thyroid Cancer

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Key Words
Thyroid bed nodules · Thyroid cancer · Thyroidectomy · Ultrasonography · ^{131}I therapy

Abstract
Objectives: We conducted a retrospective chart review of patients with differentiated thyroid cancer who underwent total thyroidectomy to examine the correlation of the persistence of thyroid bed nodules seen on ultrasonography with subsequent loco-regional recurrence. ***Methods:*** A total of 60 patients with differentiated thyroid cancer were identified who underwent total thyroidectomy, received ^{131}I therapy and had thyroid bed nodules on postoperative surveillance ultrasonography. The ultrasonographic features of the thyroid bed nodules and their progression over time along with serum thyroglobulin (Tg) levels were monitored. Those patients who demonstrated no evidence of recurrence were compared to patients who had recurrence. ***Results:*** Of the 60 patients, 25% had documented cancer recurrence. Sixty percent of the patients in the recurrence group had an increase in the size of bed nodules as compared to only 7% of the patients in the group without recurrence. An increase in serum Tg of more than 2-fold was seen in 80% of the patients with recurrence and in only 13% (6/45) of the patients without cancer recurrence. The odds of identifying recurrent thyroid cancer in patients with more than a 2-fold increase in serum Tg were 80.5 greater than in patients with a less than 2-fold increase in serum Tg. The odds of identifying recurrent thyroid cancer in patients with the presence of any suspicious thyroid bed nodule were 31.5 times greater than in patients without suspicious thyroid bed nodules. ***Conclusions:*** Thyroid bed nodules on surveillance ultrasound warrant fine-needle aspiration cytology if they increase in size and number, are persistent and associated with suspicious sonographic features.

Introduction

Differentiated thyroid cancer patients are monitored for local or distant recurrence after total thyroidectomy. They typically undergo physical examination, serial measurement of serum thyroglobulin (Tg) levels, and serial

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ultrasonography, with occasional imaging by MRI, FDG-PET or ^{131}I scanning depending on the clinical context. Neck ultrasound is recommended at 6–12 months after surgery and then less frequently depending on the risks for loco-regional recurrence [1, 2]. Approximately 20–30% of the patients with differentiated thyroid cancer have loco-regional recurrences [2]. To better predict the recurrence rate, ATA risk stratification of patients in low-, intermediate- and high-risk categories can be used. Persistent or recurrent disease has been identified in 3% of the low-risk, 21% of the intermediate-risk and 68% of the high-risk patients [3]. AJCC staging is required for all patients with thyroid cancer and postoperative clinicopathologic systems should be used for prognostication, to provide information on the risk of recurrence and to plan the follow-up of these patients [1]. Delayed risk stratification after 6–8 months of radioiodine ablation can provide more information on the risk of recurrence. Thyroid bed nodules can represent benign conditions such as neuromas, postoperative scar, suture granuloma, reactive lymphoid hyperplasia, benign thyroid tissue remnant or, instead, a malignant recurrence of thyroid cancer in which case fine-needle aspiration will show epithelial and inflammatory cells. Ultrasound helps assess which thyroid bed nodules may be malignant (with features such as micro-calcifications, increased vascularity and irregular borders) [4] but the distinction cannot be made solely based on sonographic findings, and fine-needle aspiration cytology is sometimes indicated to determine the histology [5]. Sonographic findings and Tg levels can help in identifying high-risk patients for whom fine-needle aspiration cytology will be definitely indicated to confirm cancer recurrence, whereas in low-risk patients fine-needle aspiration can be avoided. Assessment has shown that many thyroid bed nodules may not increase in size during follow-up [6] but more data are required to assess and study their significance. Hypoechoic nodules in the thyroid bed are suspicious for recurrence [7, 8]. Fine-needle aspiration of these nodules for cytologic examination is the most sensitive and specific approach to the diagnosis of cancer [9].

The purpose of the present study was to analyze the significance of thyroid bed nodules noted on neck ultrasonography postoperatively in patients with differentiated thyroid cancer. Factors that influence loco-regional recurrence were assessed and a comparison was performed of patients with recurrence and those without cancer recurrence.

Study Design

This study represented a retrospective exploratory chart review analysis. Institutional Review Board approval was obtained for the electronic chart review of ultrasonography findings of thyroid cancer patients after thyroidectomy. The authors examined the data obtained and information related to the subsequent clinical course in the patients so identified. Informed consent from the patients was waived for the study and the reviewers maintained patient confidentiality.

Participant Selection

A search engine was used to identify patients with a documented problem listed as differentiated thyroid cancer status after total thyroidectomy. A total of 60 patients were found to have the problem listed as differentiated thyroid cancer status after total thyroidectomy and had at least two postoperative ultrasound examinations with a thyroid bed nodule found on any ultrasound. Ultrasonography reports compiled at different dates were collected and retrospectively reviewed. The patients were seen at MedStar Washington Hospital Center at some point of time during their treatment course. Exclusion criteria included patients with thyroid cancer other than papillary or follicular thyroid cancer, and patients with known distant metastasis prior to the detection of thyroid bed nodules. Patients who either did not have thyroid bed nodules on postoperative ultrasonography or had less that two ultrasounds documented on follow-up visits were excluded. Patient demographics, the stage and type of cancer, serum Tg levels, size of nodule and ultrasound imaging findings were analyzed. Patients were monitored every 6 months or more frequently if they had evidence of recurrence. Patients who had laboratory studies or imaging performed at an outside hospital were included if sufficient follow-up information was available. Ultrasound reports were reviewed as the images were not available and the readings were from different operators. Patients who underwent repeat neck surgery or ^{131}I therapy any time during their treatment course were included. At the discretion of the attending endocrinologist, repeat ^{131}I therapy was performed if there was evidence of residual disease by imaging or persistent or rising serum Tg elevation. All the study patients had negative Tg antibodies.

Thyroid bed nodules were characterized based on their location (right or left), size, echogenicity, presence of macro- or microcalcifications, presence of neck lymph nodes accompanying the thyroid bed nodules, and whether or not the lymph nodes had suspicious ultrasonographic characteristics. Any neck lymph node or thyroid bed nodule was considered suspicious if it had microcalcifications, increased peripheral vascularity, loss of fatty hilum or hypoechogenicity. The size of the thyroid bed nodule was taken as the average of the three dimensions of the node. The size of the largest dimension of the largest node was also recorded. Nodules were observed over a period of time (mean duration of 10.9 years ranging over 2–35 years) to determine if they increased in size or number. An increase in size was defined as an increase in length, breadth or depth of the thyroid bed nodule by more than 3 mm, as recommended previously [6].

The subtype of differentiated thyroid cancer and the surgical pathology from the initial thyroidectomy were recorded. The size of the initial tumor foci, stage and number of neck surgeries performed were noted. The serum Tg level was monitored over time

Table 1. Characteristics of the study population

Age, years		Time from surgery to first US result available, years	
Mean ± SD	52.8±15.2	Mean ± SD	2.9±3.7
Range	18.0–93.0	Range	0–19
Female sex, %	82	Time from first to last US, years	
Type of cancer, %		Mean ± SD	6.6±3.6
Papillary	88	Range	0.0–15.0
Follicular	13	US, n	
Medullary	2	Mean ± SD	8±4
Stage, %		Range	1–23
I	67	US with thyroid bed nodule, n	
II	6	Mean ± SD	4±4
III	9	Range	1–21
IV	18	Thyroid bed nodule on first US, n	
Initial tumor foci size, cm		Mean ± SD	1±1
Mean ± SD	1.8±1.1	Range	0–3
Range	0.1–4.7	Most thyroid bed nodules on any US, n	
Surgeries, n		Mean ± SD	2±1
Mean ± SD	1±1	Range	1–5
Range	1–3	Thyroid bed nodules on first US, n	
^{131}I therapy, %	92	Mean ± SD	1±1
^{131}I therapies, n		Range	0–3
Mean ± SD	1±1	Average size of the largest nodule, mm	
Range	0–3	Mean ± SD	7.2±3.8
Total dose, mCi		Range	2.7–19.0
Mean ± SD	229.1±207.1	Largest dimension of biggest nodule, mm	
Range	0–952.0	Mean ± SD	13.8±11.5
Follow-up, years		Range	3.0–57.0
Mean ± SD	10.9±5.9	Increase in size of nodule, %	20
Range	2–35	Increase in number of nodules, %	20
Serum Tg at first US, ng/ml		Suspicious thyroid bed nodules, %	33
Mean ± SD	4.4±12.2	Suspicious neck lymph nodes, %	32
Range	0.2–70.0	Fine-needle aspiration cytology performed, %	28
Tg antibody present, %	12	Irregular thyroid bed nodule, %	7
Tg increase more than twice, %	30	Calcification in any node, %	12
Fold increase in serum Tg		Hypoechoic thyroid bed nodule, %	43
Mean ± SD	3.7±8.0	Increased vascularity in any node, %	10
Range	0.0–39.0	Absence of fatty hilum, %	5

US = Ultrasound.

to detect an increase in any dimension. Tg levels were measured at a major commercial clinical laboratory (LabCorp Inc.) by an immunochemiluminescent methodology.

Criteria for Recurrence

Out of 60 patients with thyroid bed nodules, 15 had recurrence of differentiated thyroid cancer in the thyroid bed nodule, and 45 were considered free of recurrent disease. Patients were considered to have recurrent thyroid cancer if: (1) fine-needle aspiration cytology of the thyroid bed nodule was positive at any point of time, or (2) the serum Tg level demonstrated a 2-fold or greater increase in the absence of any other structural evidence of disease, or (3) there was structural evidence of disease on other imaging studies, such as PET/CT and MRI. Patients were considered not to have disease if fine-needle aspiration cytology was negative or serum Tg levels were undetectable and there was no structural evidence of disease on any imaging studies. Fine-needle aspiration cytology was not performed in some patients who were considered to have recurrent thyroid cancer based on their Tg levels and evidence of structural disease, but in whom any intervention to change the outcome was not indicated.

Statistical Analysis

Univariate statistics was used to study the characteristics of the population. Means and standard deviations of the continuous variables and percentages and frequencies of the categorical vari-

ables were calculated. For the continuous variables, the difference in the averages was tested using t test when the normality assumption was satisfied, and using the nonparametric Wilcoxon test when the normality assumption was not satisfied. For categorical variables, difference in the proportions was examined by χ^2 and Fisher exact tests. $p < 0.05$ was considered to indicate a significant difference.

Multivariate logistic regression analysis was conducted to determine the factors that affect cancer adjusting for the identified potential confounding factors. A backward elimination method was used to remove one nonsignificant effect in each step. $p < 0.05$ was considered significant.

Results

Characteristics of the study population are given in table 1. The mean age of the study population was 52.8 years (range 18–93) with the majority being women (82%). Papillary cancer accounted for 88% of the cases. Out of 28 patients who had a pathologic documentation of the variant of papillary thyroid cancer in their medical record, the majority had the follicular variant of papillary thyroid cancer (13 patients), others had the classical variant (4 patients), tall cell variant (4 patients), Hurthle cell variant (5 patients), sclerosing variant (2 patients) and columnar type of papillary thyroid cancer (1 patient). One patient had both the follicular and papillary variant of thyroid cancer on histology.

The majority of the patients in the study were found to have stage I cancer (67%), with the second most common being stage 4 (18%). The staging was done based on the patient status at the time of review. Initial therapy in these patients included total thyroidectomy and 55 patients had postoperative ^{131}I ablation (mean cumulative dose of 229.1 ± 207 mCi, range 0–952). Fifteen patients in the study had repeat surgery and 21 patients received repeat ^{131}I therapy if residual disease was suspected or if there was a concern for recurrence based upon results of imaging or laboratory studies, such as persistently elevated serum Tg levels. Fine-needle aspiration cytology of either neck lymph nodes or thyroid bed nodules was performed in 17 out of the 60 patients. The mean follow-up duration from the time of surgery until the last clinic visit was 10.9 years (range 2–35).

Table 2 summarizes the outcomes of loco-regional occurrence and comparison between patients with and without recurrence. During the course of follow-up, an increase in the size of a thyroid bed nodule (defined as a more than 3 mm increase in any dimension) was noted in 20% patients and an increase in the number of thyroid bed nodules (defined as an increase in number by more than or equal to one) was noted in 20%. Out of 60 patients with a thyroid bed nodule, 20 patients had a suspicious-appearing thyroid bed nodule and 19 had suspicious neck nodes based upon ultrasonographic criteria. An increase in serum Tg of at least 2-fold was noted in 18 patients, with 12 being patients with regional recurrence.

Four patients were considered to have disease even though no fine-needle aspiration cytology had been performed. One patient was considered to have disease as she had a lung metastasis on other imaging studies but the lesion was too small to biopsy. She had other clinical indicators suggestive of malignancy, such as a 22-fold increase in serum Tg. Another patient was considered to have disease as she had persistent enlarged neck lymph nodes, an increase in the size of bed nodules, persistently positive serum Tg and a 39-fold increase from the baseline serum Tg. A fine-needle aspiration cytology performed in this patient was suspicious for malignancy. One patient had an increase in the size of bed nodules with a 15-fold increase in serum Tg and had suspicious nodes with microcalcifications and heterogeneity. Another patient had a 22-mm bed nodule with persistently elevated serum Tg (ranging between 2 and 8 ng/ml with an rhTSH-stimulated serum Tg of 64 ng/ml) and suspicious neck nodes consistent with cancer recurrence in the thyroid bed nodule. She was considered to have disease but no fine-needle aspiration cytology was performed given the clinical context of the patient and that any intervention to change the outcome was not indicated.

Loco-Regional Occurrence

Table 2 summarizes the outcomes of loco-regional occurrence and comparison between patients with and without recurrence. The age, sex and type of cancer were similar in the two groups, but there were important significant differences noted. The size of the initial tumor foci was greater and the stage of the thyroid cancer was higher in patients with recurrence ($p = 0.0171$). Patients with recurrence required a greater number of surgeries (1.4 ± 0.5), ^{131}I therapies (2.1 ± 0.8) and mean cumulative doses of radioactive iodine (RAI). Statistically significant differences were seen in the characteristics of thyroid bed nodules. Sixty percent of patients (9/15) in the recurrence group had a significant increase in the size of thyroid bed nodules as compared to only 7% (3/45) in the group without recurrence ($p < 0.001$). In addition, 60% of the patients with recurrence had an increase in the number of nodules as compared to 7% in the nonrecur-

Table 2. Comparison of patients with thyroid bed nodules with and without differentiated thyroid cancer recurrence (bivariate analysis)

Characteristics of the study population	Patients without cancer recurrence (n = 45)	Patients with cancer recurrence (n = 15)	p value
Age, years	51.1±13.7	57.9±18.6	0.1332
Female	36 (80)	13 (87)	0.7138
Type of cancer			
Papillary	40 (89)	13 (87)	1.0000
Histology follicular	6 (13)	2 (13)	1.0000
Stage			0.0003
1	35 (81)	2 (17)	
2	1 (2)	2 (17)	
3	3 (7)	2 (17)	
4	4 (9)	6 (50)	
Initial tumor foci size, cm	1.6±1.0	2.5±0.9	0.0171
Surgeries (total thyroidectomy), n	1±0	2±0	0.0380
^{131}I therapy	40 (89)	15 (100)	0.3180
^{131}I therapies, n	1±1	2±1	0.0001
Total dose of ^{131}I therapy, mCi	157.3±131.0	413.8±253.7	0.0010
Follow-up duration, years	9.8±4.4	14.1±8.5	0.0158
Time from surgery to first US, years	2.1±2.5	5.3±5.5	0.0153
Time from first to last US, years	6.0±3.0	8.4±4.7	0.0277
US, n	7±4	10±6	0.2518
US with thyroid bed nodule, n	3±2	7±6	0.0067
Thyroid bed nodules on first US, n	1±1	1±1	0.5302
Most thyroid bed nodules on any US, n	1±0.6	2±1.3	0.0018
Thyroid bed nodules on first US, n	1±0.7	1±1.0	0.5814
Average size of first thyroid bed nodule, mm	5.7±3.9	7.4±4.6	0.1172
Average size of largest thyroid bed nodule, mm	5.8±2.3	11.4±4.4	<0.0001
Largest dimension of biggest node, mm	12.6±12.1	17.1±9.1	0.0034
Tg antibody present	5 (11)	2 (13)	1.0000
Serum Tg increase (more than 2-fold)	6 (18)	12 (80)	<0.0001
Increase in size of thyroid bed nodules	3 (7)	9 (60)	<0.0001
Increase in number of thyroid bed nodules	3 (7)	9 (60)	<0.0001
First thyroid bed nodule suspicious	7 (16)	10 (67)	0.0001
Any thyroid bed nodule suspicious	8 (18)	12 (80)	<0.0001
Any neck lymph node suspicious	7 (16)	12 (80)	<0.0001
Fine-needle aspiration cytology performed	5 (11)	12 (80)	<0.0001
Irregular thyroid bed nodules present	1 (2)	3 (20)	0.0448
Any calcification in thyroid bed or neck node	2 (4)	5 (33)	0.0083
Hypoechoic thyroid bed nodule	15 (33)	11 (73)	0.0143
Increased vascularity	2 (4)	4 (27)	0.0298
Absence of fatty hilum	1 (2)	2 (13)	0.1514

Data are mean ± SD or n (%). US = Ultrasound.

rence group ($p < 0.001$). A serum Tg increase of more than 2-fold was noted in 80% of the patients with recurrence (12/15). In the nonrecurrence group, only 18% (6/45) had an increase in serum Tg level of more than 2-fold ($p < 0.05$).

Multivariate analysis (table 3) also showed statistically significant differences. As shown in table 3, the odds of identifying thyroid cancer in patients with more than a 2-fold increase in serum Tg was 80.5 times greater than in patients with less than a 2-fold increase in serum Tg ($p = 0.0018$). Table 4 shows that if the serum Tg increases

Table 3. Multivariate analysis: analysis of effect

Effect	DF	Wald χ^2	Pr > χ^2 (p value)	Point estimate (odds ratio)
More than 2-fold increase in serum Tg	1	9.7321	0.0018	80.471
Any thyroid bed nodule suspicious	1	7.3014	0.0069	31.469

DF = Degrees of freedom.

Table 4. Sensitivity, specificity, PPV and NPV of different parameters

Parameters	Sensitivity, %	Specificity, %	PPV, %	NPV, %
Serum Tg increase	92	80	60	97
Serum Tg increase more than 2-fold	92	85	67	97
Increase in nodule size	60	93	75	88
Any suspicious nodule (thyroid bed/neck lymph node)	80	82	60	92
Combination of increase in serum Tg and nodule size	47	100	100	85

PPV = Positive predictive value; NPV = negative predictive value.

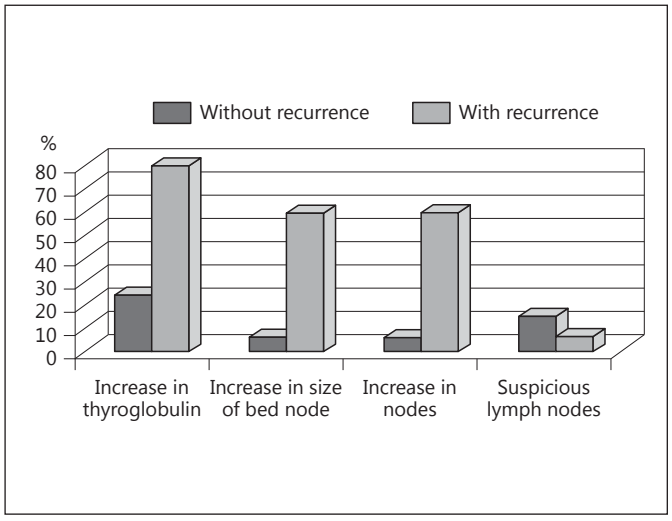

Fig. 1. Summary of the results.

by more than 2-fold, the sensitivity of detecting a thyroid cancer recurrence is 92% with a specificity of 85%. The positive predictive value for more than a 2-fold increase in serum Tg in detecting thyroid cancer recurrence is 67% and the negative predictive value is 97%. The graph shown in figure 1 summarizes the results.

Discussion

Papillary thyroid cancer accounts for about 85% and follicular cancer accounts for about 15% of the differentiated thyroid cancer cases [10]. The criteria for the absence of cancer recurrence after total thyroidectomy include no clinical evidence of disease on imaging studies and laboratory studies, such as undetectable serum Tg levels during TSH suppression and stimulation [1]. A change in the morphology of a thyroid bed nodule and/or appearance of enlarged neck lymph nodes after thyroidectomy are important predictors of recurrence and are usually accompanied by increases in serum Tg levels [11].

Suspicious cervical lymph nodes more than 5–8 mm in their smallest dimension should undergo fine-needle aspiration cytology while cervical lymph nodes less than 5–8 mm in the largest dimension can usually be followed up without biopsy [1]. The 2013 European Thyroid Association guidelines for the use of cervical ultrasonography in the postoperative management of patients with thyroid cancer suggest fine-needle aspiration of suspicious-looking thyroid bed nodules >1 cm in size or for which growth has been documented, while surveillance monitoring can be chosen for small or stable lesions [12]. The present study indicates that an increase in the size of a thyroid bed nodule (by more than 3 mm in the largest

dimension) suggests thyroid cancer recurrence with a high positive predictive value. The increase in the size of thyroid bed nodules seen in 20% of the patients is higher than in a previous study when an increase in the size of thyroid bed nodules was noted in 9% of the cases [6]. This difference is possibly attributed to a longer follow-up time from the first to last ultrasound in the present study, with a mean follow-up time from the first to last ultrasound of 6 years in the group without cancer recurrence versus 8 years in patients with recurrence. In the present study, a 3-mm increase in the size of the thyroid bed nodule was considered significant and this criterion has been documented in the literature in the past. This may not be applicable to a macroscopic thyroid bed nodule that is several centimeters in size which subsequently undergoes only a 3-mm increase that is not likely to be significant. The majority of nodules in this study were sub-centimeter and the average size of the first thyroid bed nodule detected in the group without recurrence was similar to the group with recurrence (5.7 ± 3.9 vs. 7.4 ± 4.6 mm, respectively; $p = 0.1172$). The present study also had a relatively high number of patients with biopsy-proven cancer recurrence (11 out of 15 patients with recurrence). The size of thyroid bed nodules, both the average ($p < 0.001$) and the largest dimension ($p = 0.003$), was found to be important in assessing recurrence, as was the nodule configuration, with irregular large heterogeneous thyroid bed nodules representing a higher chance of thyroid cancer recurrence. These results are in concurrence with those of Rondeau et al. [6]. In their study, as in our findings, the majority of thyroid bed nodules were observed to be benign and to tend to grow slowly even when malignant.

Any suspicious features in a thyroid bed nodule along with suspicious neck lymph nodes suggest consideration for fine-needle aspiration cytology as they have a higher chance of recurrence with a 60% positive predictive value, as indicated by identifying the 11 patients in the study with fine-needle aspiration cytology-proven recurrence of thyroid cancer. Based on our results on multivariate analysis that suspicious thyroid bed nodules have an odds ratio of 31.5 for cancer recurrence, we conclude that patients without any increase in size or number of bed nodules, with stable serum Tg levels and benign morphology of neck lymph nodes on ultrasonography can be monitored over time without further intervention. This approach is supported by the negative predictive value of 85% for a combined increase in size and a doubling in serum Tg. Although conclusions are limited by a relatively small number of patients, the present study also indicates that patients with recurrence have a higher number of bed nodules and the nodules persist for longer. It will be important to look at the time period after surgery when the thyroid bed nodules are identified on ultrasonography. This was not performed in this study but may help in differentiating a benign lesion from cancer recurrence. The presence and size of benign thyroid bed nodules will vary, probably related to the vicissitudes of factors, such as differing radiologist interpretation and equipment used. We would expect that most patients with loco-regional recurrence will have an increase in serum Tg and in the size of bed nodules, although 2 patients with loco-regional cancer recurrence in this study did not have an increase in serum Tg levels or increase in the size of bed nodules. In these patients the diagnosis was made by CT scan and later fine-needle aspiration cytology performed for a stable thyroid bed nodule of more than 1 cm in size.

Review of the ultrasound reports demonstrated that information was often limited on the morphology of the neck nodes in regard to vascularity and loss of fatty hilum. Variability in ultrasonography findings are dependent on both the equipment employed and the technique of the operator. Moreover, minor changes can be seen in thyroid bed nodules over a period of time with unclear significance. The histologic variant of papillary cancer plays an important role in outcome, especially the tall cell variant that is associated with poor prognosis [13]. Although the present study included both papillary and follicular thyroid cancer with similar prognosis and staging [10], the differences in their respective growth and metastatic patterns need to be considered when evaluating the significance of thyroid bed nodules [14].

Serum Tg levels are typically measured every 6–12 months by an assay that is calibrated with the standard CRM-457 assay and are useful after either thyroxine withdrawal or rhTSH stimulation 12 months after RAI ablation [1]. In the absence of Tg antibodies, an undetectable serum Tg when the serum TSH is stimulated excludes residual cancer in more than 99% of the cases [15]. Twenty percent of the patients who are clinically free of disease with serum Tg <1 ng/ml on TSH suppression will have a serum Tg level >2 ng/ml after rhTSH at 12 months after therapy [1]. One third of these patients will have recurrent or persistent thyroid cancer and increasing serum Tg levels [16]. If stimulated serum Tg levels rise to >2 ng/ml, imaging of the neck should be performed [1]. If there is no evidence of disease on imaging, the patients with stimulated serum Tg <5 ng/ml with rhTSH can be monitored over time. Aspiration cytology biopsy needle wash Tg lev-

els complement cytology in diagnosing cancer [17]. Serum Tg levels are also higher in thyroid bed recurrence versus distant metastasis. In patients with positive Tg levels but a negative RAI scan, imaging such as CT, MRI or FDG-PET can be helpful. FDG-PET can be falsely positive in patients with granuloma or inflammatory lymph nodes in the thyroid bed and is more helpful in high-risk patients [1]. The present study indicates high sensitivity, negative predictive value and odds ratio for finding recurrence when a more than 2-fold increase in serum Tg levels occurs. Patients with Tg antibodies have unreliable serum Tg levels [1, 15]. The patients in the study were negative for Tg antibodies. It is recommended to measure serum Tg in an individual patient over time in the same assay because of the differences observed between various assays [18].

Patients in the present study with recurrence had a longer follow-up (mean 14 years) as compared to patients without recurrence, which suggests slow growth and recurrence of thyroid cancer. Patients in the study with a higher cancer stage and greater tumor burden had higher chances of recurrence. One of the possible explanations for the observation that the number of ^{131}I treatments and the cumulative doses of ^{131}I therapy were higher in the recurrence group is that the patients with recurrence were followed up for longer and were managed with ^{131}I therapy or surgery as deemed clinically indicated. Data on the extent of neck dissection on repeat surgery was not recorded. This can affect the recurrence rate in the thyroid bed. The occurrence of thyroid bed nodules was not studied in relation to the ^{131}I therapy. The timing of ^{131}I therapy in relation to the appearance of thyroid bed nodules can impact the incidence and occurrence of cancer in the nodules. The intensity of follow-up was noted to vary, with patients with recurrence being followed more closely and having a higher number of ultrasound examinations.

Conclusion

Thyroid bed nodules on surveillance ultrasound may warrant fine-needle aspiration cytology if they increase in size and number, are persistent and are associated with suspicious features on ultrasound. In the presence of thyroid bed nodules, an increase in serum Tg levels by more than 2-fold is worrisome for cancer recurrence. Irregular heterogeneous hypoechoic thyroid bed nodules with increased vascularity have a higher chance of thyroid cancer recurrence.

Disclosure Statement

Dr. Wartofsky has served as a Consultant to Genzyme, Eisei, Asuragen/Interpace, and IBSA.

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