

Is Fine Needle Aspiration Biopsy Effective in Detecting Malignancy in Giant Thyroid Nodules?

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ABSTRACT

Thyroid fine needle aspiration biopsy (TFNAB) is the most important diagnostic method to determine malignancy in thyroid nodules. However, it is effectiveness in diagnosing malignancy in large thyroid nodules (greater than 4 cm) is controversial. In this study, we compared the postoperative histopathological results of 147 patients who had thyroid nodules greater than 4 cm and underwent surgery with preoperative ultrasonography and FNAB findings. In our study, we aimed to evaluate the efficacy of FNAB in giant thyroid nodules.

147 patients who were operated in our general surgery clinic for a thyroid nodule with a diameter of 4 cm and above we included in the study. The patient's data gender, age, preoperative laboratory findings, thyroid imaging results, FNAB reports and postoperative histopathology results were evaluated.

Of 147 patients, 116 were female and 31 were male. The mean age of patients was 48.14 years. Thyroid ultrasonography revealed isoechoic heterogeneous in 95 patients, hypoechoic in 32 patient and hyperechoic heterogeneous in 20 patients. Microcalcification was detected in 44 patients, microcalcification in 32 patients, and peripheral calcification in 18 patients.

Biopsy results were reported as benign in 99 patients, aspiration of uncertain significance in 19 patients, follicular-nodular hyperplasia in 4 patients, suspected malignancy in 9 patients, and malignancy in 4 patients. The results of 110 patients were reported as benign in the postoperative histopathological examination. Papillary carcinoma was detected in 34 patients, follicular carcinoma in 2 patients, lymphoma in one patient, Hashimoto's thyroiditis in 5 patients, and Graves' disease in 5 patients.

Postoperative histopathology results of 4 patients whose FNAB results were reported as malignant were also malignant (100%). The preoperative FNAB could not detect the malignancy in 33 patients whose postoperative histopathology results were malign. The most significant parameters in detecting malignancy with ultrasonography were evaluated as increased vascularity, wall irregularity and hypoechoic heterogeneity, respectively. Ultrasonography was found to be more significant than FNAB for the detection of malignancy in giant thyroid nodules in our study.

Keywords: Thyroid nodule, ultrasonography, biopsy, malignancy.

Introduction

Thyroid cancers constitute approximately 1% of all cancers. However, they are the most common cause of endocrine cancers (1). It is seen as three times more common in women than men. Although they are most commonly between the ages of twenty and forty, they can occur in any age group (2). Most of the nodules formed in the thyroid gland do not show symptoms. Even if these nodules are asymptomatic, they cannot be accepted to be benign (3). Thyroid ultrasonography (USG) and Thyroid Fine Needle Aspiration Biopsy (TFNAB) should be performed in the approach to thyroid nodules, whether they are symptomatic or not. Especially an increase in antero-posterior diameter, hypoechoogenicity,

microcalcification, nodule wall irregularity, increased vascularity, and increased strain index in elastasonography in addition to the size of the nodule on USG is interpreted in favor of malignancy (4). Currently, FNAB is considered the most important diagnostic tool in differentiating malignant and benign thyroid nodules. The decision of surgery or clinical follow-up for a patient is made according to the FNAB results. Cytology materials obtained by FNAB are divided into six categories according to Bethesda classification: non-diagnostic, benign, aspiration of uncertain significance, follicular neoplasia, suspected malignancy, and malignant (5). Surgical treatment should be done for patients with malignant FNAB results. Patients with benign results can be followed with USG. A repeat FNAB is appropriate when an

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increase in nodule size or a change in nodule character is detected. A relationship was found between nodule size and cancer (6). Despite this data, there are also studies stating that the efficacy of FNAB is low in thyroid nodules of 4 cm and above (7,8).

In our study, we aimed to investigate whether FNAB is sufficient when making a decision for surgery in patients with thyroid nodules of 4 cm and larger. We compared the effectiveness of USG with FNAB.

Material and Methods

The data of 446 patients who were operated for thyroid nodules in Seyhan State Hospital General Surgery Clinic between January 2010 and December 2022 were analyzed. 147 (32.95%) patients out of these 446 cases who were operated for 4 cm and larger were included in the study. The patients' gender, age, preoperative laboratory results, imaging findings, biopsy and postoperative pathology results were evaluated. The data of the patients were revealed from the electronic databank. Patients with a history of preoperative neck radiation and lymph node involvement were excluded from the study. Recurrent patients who had previously been operated for thyroid disease were also excluded from the study. All patients had thyroid hormone tests, USG and TFNAB preoperatively. Patients who did not meet these criteria were excluded from the study. Thyroidectomy was performed in patients whose FNAB results were reported as insufficient samples twice. Ethical consent for his study was obtained from University of Health Sciences, Adana City Education and Research Hospital Ethical Committee.

Statistics: Statistical Package for Social Science for Windows (SPSS) 24.0 package program was used to evaluate the data obtained in the study. Frequency and percentage distribution analysis was used to determine the gender distribution of the descriptive features of the patients evaluated in the study, and the mean and standard deviation values were examined for the determination of age, T3, T4 and TSH values. In order to examine the statistically significant differences of T3, T4 and TSH values in terms of biopsy and pathology results, the independent sample t-test (Independent t-Test) was applied in the study. Chi-square test analyzes were applied in order to examine whether the patients showed a statistically significant change in terms of gender, complaints, USG findings, and pathology results, which is the main purpose of the analysis. The results were considered significant at 99% ($p < 0.01$) and 95% ($p < 0.05$) confidence levels.

Results

147 of 446 patients who were operated for thyroid nodule disease had a nodule diameter of 4 cm and above. 116 of these 147 patients were female (78.9%) and 31 ones were male (21.1%). The mean age of patients was 48.14 (Table 1). The mean of TSH values was 1.97 ± 1.14 , T3 values 3.57 ± 0.97 and T4 values was 0.97 ± 0.36 . Bilateral total thyroidectomy was performed in 4 patients with malignant FNAB results and 9 patients with suspected malignancy, and bilateral near-total subtotal thyroidectomy was performed in 64 patients with multiple nodules. Forty-four patients with nodules in only one lobe underwent bilateral total thyroidectomy in their choice of treatment. The remaining 26 patients underwent right or left lobectomy. Complementary total thyroidectomy was performed in 8 of these 26 patients whose histopathological results were reported as papillary cancer.

The mean antero-posterior nodule diameter in thyroid USG was 5.4 ± 0.46 cm. There was isoechoic heterogeneity in 95 patients, hypoechoic in 32 patients, and hyperechoic heterogeneity in 20 patients in USG examination. Microcalcifications were detected in 44 patients, macrocalcifications in 32 patients, and peripheral calcifications in 18 patients. While 12 patients had both microcalcification and macrocalcification, 6 patients had microcalcification, macrocalcification and peripheral calcification together. There was wall irregularity in 12 patients and increased vascularization in 14 patients (Table 2). Biopsy results of 99 patients who underwent FNAB were reported as benign, 19 with uncertain aspiration, 4 with follicular-nodular hyperplasia, 9 with suspected malignancy, and 4 with malignancy. 110 (74.8%) of 147 patients were reported as benign and 37 (25.2%) were reported as malignant in the histopathological examination. Of 37 patients reported as malignant, 34 were papillary carcinoma, 2 were follicular carcinoma, and one patient was lymphoma.

The reports which were reported as benign was Hashimoto Thyroiditis in 5 patients and Graves disease in 5 patients (Table 3).

When the data were examined, there was no statistically significant relationship between the age and gender of the patients and malignancy. The incidence of malignancy was higher in female patients. Although TSH values were higher in the malignant group than in the benign group, no statistically significant difference was found. T3 and T4 values were similar in both groups.

There was an isoechoic pattern in 95 patients on USG. Histopathologically, malignancy was detected in

Table 1: The Demographic Characteristics of the Patients

Gender	Number	Mean of age (years)	Percent (%)
Female	116	46.16	73.09
Male	31	50.12	16.01
Total	147	48.14	

Table 2: The Sonographic Characteristics of The Thyroid Nodules

	N/%	Histopathology					p	
		Bening	Papiller ca	Follicular ca	Lymhoma	Graves		Hashimoto
Isoechoic	95(%64.62)	92(%96.84)	3(%3.15)			3(%3.15)	2(%2.10)	0.831
Hypoechoic	32(%21.76)	22(%68.75)	10(%31.25)					0.913
Hyperechoic	20(%13.60)	15(%75.00)	2(%10)			2(%10)	1(%5)	0.816
Microcalcification	44(%29.93)	40(%90.90)	4(%9.09)					0.822
Macrocalcification	32(%21.76)	26(%81.25)	3(%9.37)		1(%3.12)		2(%6.24)	0.986
Wall irregularity	12(%8.84)	6(%46.15)	6(%46.15)	1(%7.69)				0.871
Increased vascularity	14(%9.52)	7(%50)	6(%42.85)	1(%7.14)				0.815
Total	147	110(%74.82)	34(%23.12)	2(%1.36)	1(%0.68)	5(%3.40)	5(%3.40)	0.986

only 3 of these 95 patients. Histopathologically, malignancy was seen in 10 (31.25%) of 32 hypoechoic patients. Although this rate was higher, it was not statistically significant. On the other hand, malignancy was detected in only 2 of the 20 patients with hyperechogenicity. These results were not statistically significant. There was malignancy in 4 (9.09%) of 44 patients with microcalcifications. However, malignancy was detected in 3 (9.37%) of 32 patients with macrocalcification. Malignancy was present in 7 (53.84%) of 13 patients with wall irregularity, and although this rate was high, it was not statistically significant. Similarly, malignancy was detected histopathologically in 7 (53.84%) of 13 patients with increased vascularity. Although this rate was high, it was not statistically significant.

Histopathological evaluation of 82 (82.8%) of 99 patients with benign FNAB results showed also benign findings, however, the pathology of 12 patients (12.1%) was malignant. The histopathology of 4 patients with malignant FNAB was also malignant. This was found statistically significant.

While the sensitivity of FNAB was 100%, false-negativity was found to be 12.1%. Malignancy was detected histopathologically in 4 (44.44%) of 9 patients with suspected malignancy. Only one patient out of 4(25%) who had diagnosis of follicular hyperplasia was reported as malignancy. In the postoperative pathology report of 14 patients who were reported as non-diagnostic in FNAB, only 5 (35.71%) cases had detection of the diagnosis of malignancy. These results were not statistically significant. Malignancy was detected in 15 (78.94%) of 19 patients who had the result of aspiration of uncertain significance, and this high rate was statistically significant.

Discussion

Thyroid nodules are common in some geographic areas. They are most commonly seen in female patients aged 50 years, also it is possible to encounter thyroid nodules in approximately half of people of this age (9). The rate of female patients in our study was 78.9%. The mean age of our patients was 48.14,

Table 3: Comparison of FNAB Results of The Thyroid Nodules With Postoperative Histopathology

FNAB	N/%	HISTOPATHOLOGY						p
		Bening	Papillary ca	Follicular ca	lymphoma	graves	hashimoto	
Bening	99(63.1)	82(82.8)	12(12.1)	-	-	3(3.03)	2(2.02)	0.964
Non diagnostic	14(14.1)	7(50)	4(28.57)	-	1(7.42)	1(7.42)	1(7.42)	0.012
AUS	19(12.1)	5(26.31)	10(52.63)	1(5.26)	-	-	2(10.52)	0.595
Follicular neoplazi	4(2.5)	2(50)	1(25)	-	-	1(25)	-	0.756
Suspected malignancy	9(5.7)	5(55.55)	3(33.33)	1(11.11)	-	-	-	0.368
Malignant	4(2.5)	-	4(100)	-	-	-	-	0.010
Total	147	110(70.1)	34(21.7)	2(1.3)	1(0.6)	5(3.2)	5(3.2)	0.847

AUS: Aspiration of Undetermined Significance

which was consistent with the literature. There is no consensus for the definition of the giant nodule. Nodules of 4 cm and above are defined as giant nodules in some studies, while there are studies that define this as 6 cm and above (10,11). We defined the nodules of 4 cm and above as giant ones in our study. Although it is assumed that there is a relationship between nodule diameter and malignancy in the studies in the literature, this rate varies between 7.8% and 58.6% (12-13). In our study, 37 of 147 patients (25.17%) had malignant histopathology. In our study, the histopathology of 4 patients with malignant FNAB was also malignant. Therefore, the accuracy rate was 100%. However, the histopathology of only 4 of 9 patients with suspected malignancy was malignant. Therefore, our accuracy rate was 91.15%. The accuracy rates in the literature vary between 82 to 100%. Therefore, our result was consistent with the literature (14, 15). There was no false negativity in our study. However, histopathology of 12 of 99 patients with benign FNAB was malignant. Therefore, our false negative rate was 12.1%. However, 8 of these 12 patients had more than one nodule and biopsy was performed on the largest nodule which was the dominant nodule.

Thus, the false negative rate may have increased. This rate is about 5% in small nodules, while this rate is as high as 13% in large nodules in the literature (16,17). At the same time, TFNAB efficacy may be lower in large thyroid nodules (18). Our false negative rate was found to be 12.1% which was compatible with the literature. Although it was not statistically significant, the false-negative rate of FNAB was high in large

thyroid nodules and we found that its effectiveness was decreased.

However, we did not have a false positive case in our study.

Cytology is the most important determinant when deciding on surgery for thyroid nodules. However, there is an increasing number of studies advocating that ultrasonography should be used to evaluate the patients with large thyroid nodules due the decrease in the diagnostic value of cytology (19,20). In a study by Kiziltan et al evaluated the comparison of FNAB and paraffin section results and found that diagnostic analysis of intraoperative FNAB for thyroid cancer revealed 33.33% sensitivity, 100% specificity and 94.59% overall accuracy (21).

Rapid enlargement of the nodule, hypoechogenicity, irregular contours, presence of microcalcifications, no change in shape upon compression, greater anterior-posterior diameter, thick and irregular wall, and increased blood supply are significant in favor of malignancy. Among these sonographic features, the rapid enlargement of the nodule, hypoechogenicity, irregular contours and the presence of microcalcifications have higher sensitivity and positivity than others. It is reported that the more of these criteria, the more likely that nodule will be malignant (22). In our study, papillary cancer was detected in 10 (31.25%) of 32 hypoechoic patients as a result of histopathology. Although this rate was high, it was not statistically significant. In our study, only 4 (9.09%) of 44 patients with microcalcifications on USG had papillary ca, and this rate was similar to the rate of malignancy in patients with

macrocalcification. At the same time, it was not consistent with the data in the literature (23,24). Papillary ca was detected in 6 (46.15%) of 13 patients with wall irregularity and follicular ca was detected in one patient (7.69%) histopathologically. Although this rate was high, it was not statistically significant. However, it was consistent with other studies in the literature. (24,25). Histopathologically, 7 (50%) of our 14 patients with increased vascularity were reported as papillary ca and one (7.14%) as follicular ca. This rate was the most significant criterion for determining malignancy in USG in our study and it was similar to the literature (25).

The most important criteria for detecting malignancy on USG in our study were increased vascularity, wall irregularity, and the presence of hypoechoic nodules or nodules, respectively. We could not detect a difference between microcalcification and macrocalcification criteria.

It was found in our study that although the sensitivity of TFNAB performed in thyroid nodules larger than 4 cm was high, false negativity was also found to be high. We concluded that USG alone is insufficient to detect malignancy in these patients. It would be useful to evaluate USG and FNAB together when making the surgical decision, especially in patients with non-symptomatic giant thyroid nodules. It would be appropriate to follow up the patients with USG and to perform a biopsy on the patients with suspected malignancy. New algorithms are needed to evaluate patients with giant thyroid nodules. USG alone is not sufficient to evaluate these patients.

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