Ultrasound Guided-Fine Needle Aspiration Biopsy of Thyroid Nodules: 18 Months Retrospective Review of One Center Experience

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Abstract

The objective of this study is to elucidate the use of ultrasonography guided fine-needle aspiration biopsies (UG-FNAB) in the evaluation of thyroid nodules. The study population consisted of 790 UG-FNAB in 719 patients whom were admitted to the our endocrinology clinic. The cytological results were classified as benign, follicular lesion or suspicious for malignancy, malignant and non-diagnostic. The results of 790 UG-FNAB of 719 patients were as follows: 567 (71.77%) benign, 97 (12.28%) non-diagnostic cytology, 43 (5.44%) atypia with undetermined significance, 81 (10.25%) follicular lesion or suspicious for malignancy, 2 (0.25%) malignant. In our study, thyroid carcinoma rate was found to be lower than current literature. Of the malignant nodules which were reported as papillary thyroid carcinoma by UG-FNAB cytology, both were female, euthyroid and have single nodule in their thyroid gland. One of the patient (39 years old) had a micro nodule (< 1 cm in diameter) that it had an isoechoic pattern with regular margin on thyroid ultrasonography; whereas the other one (79 years old) had macro nodule (>1 cm diameter) that it had, hypoechoic pattern with irregular margin. None of them have calcifications in their nodules. Multidisciplinary approach including endocrinologists, radiologists and pathologists is essential for the management of patients with thyroid nodules to avoid missestimation of the risk of thyroid cancer.

Key words: Thyroid nodules, ultrasound, fine needle aspiration biopsy, histopathology

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Introduction

It was reported that 50% of the population have thyroid nodules verified by ultrasonographic examination [1]. Although thyroid nodular disease is common, especially among women, only a limited number of nodules are malignant. Thyroid cancer accounts for 1% of all malignancies [2,3]. Ultrasound guided-fine needle aspiration biopsy (UG-FNAB) is the most preferred method in the evaluation of thyroid nodules. UG-FNAB has proven to be an important and widely accepted, cost-effective, simple, safe, and accurate method for triaging patients with thyroid nodules [4]. Approximately, 5% of nodules are malignant [5,6]. UG-FNAB is effective for differentiating malignant thyroid nodules from benign.

The primary aim of this study was to elucidate the use of ultrasonography guided fine-needle aspiration biopsies (UG-FNAB) in the evaluation of thyroid nodules. The secondary aim was the compare ultrasonography features of the benign nodules with malign nodules.

Materials and Methods

Patients admitted to Outpatient Clinic of Endocrinology Department of Samsun Training and Research Hospital with thyroid nodules from October 2011 to May 2013 (18 months) were included in the study. 790 UG-FNAB specimens from 719 patients were evaluated retrospectively.

Biopsy procedure: After physical examination, the patient was kept in the supine position with hyperextension of the neck with a rolled pillow. The nodule is localized with a 10 MHz transducer prior to biopsy. The overlying skin is cleansed with iodine. Local anesthetic, lidocaine sprey (Vemcaine® 10% pump sprey) was routinely administered to the neck region of the skin. Sampling was carried out using a fine needle (caliber 22 Gauge), manual aspiration and a 5- 10 ml syringe. Once the needle was introduced into the solid part of the nodule, negative syringe pressure was applied. After aspiration, smear was placed on slides and air-dried. Two to three slides from each patient were stained with Wright-Giemsa stain to confirm the presence of follicular cells. The slides were subsequently stained with May-Grünwald-Giemsa stain.

Physical examination, UG-FNAB, and clinical follow-up of the patients were carried out by the same physician. Informed and signed consent were obtained from all patients. No serious complications were seen during the procedure.

Ultrasonographic features of the nodules were evaluated and recorded by the experienced radiologists in our hospital.

FNAB results, classified according to the Bethesda 2010 recommendations (The Bethesda System for Reporting Thyroid Cytopathology - TBSRTC categories), in order to optimize diagnostic and therapeutic management of nodules [7]. FNAB results were classified into 5 groups as benign, suspicious for malignancy, malignant, atypia with undetermined significance, and non-diagnostic cytology. Pathological investigations were carried out by experienced pathologists in our hospital. Furthermore, we compared US finding and cytological result of UG-FNAB specimens in patients underwent thyroidectomy operations.

Statistical analyses were performed by using x2 test with Statistical Package for Social Sciences (SPSS for Windows, version 15; Chicago; IL).

Results

A total of 719 patients with mean age 51.59 ±13.83 years (range 16–90 years) were investigated. Of these 103 (14.3 %) were male (mean age 56.05 years; range 21–86 years), and 616 (85.7%) were female (mean age 50.84 years; range 16–90 years). 503 patients (70%) were in euthyroid, and 106 patients (14.7%) were hyperthyroid, whereas 110 patients (15.3%) were hypothyroid status.

In 295 (41%) of the patients, there were only one nodule; in 49 (6.8 %) of patients there were 2 nodules; and in 375 (52.2 %) of patients there were 3 or more nodules. 274 (38.1%) nodules were solid, whereas 61 (8.5%) of had cystic, and 384 (53.4 %) of had solid and cystic (mixed) pattern. 407 (56.6%) of the nodules were > 1cm, and 54 (7.5%) were around 1 cm, 258 (35.9%) were < 1cm diameter on ultrasonographic evaluation. 604 nodules were hypoechoic (84%), 82 were isoechoic (%11.4), and 33 were hyperechoic pattern on ultrasonographic evaluations. 108 (15%) of 719, had macro; 11 (1.5%) of had microcalcifications. 700 (97.4%) of them had regular margin whereas 19 (2.6 %) had irregular (Table1).

106 patients (14.7 %) had been using levothyroxine therapy for hypothyrodism, and 15 (2.1 %) antithyroid therapy for hyperthyroidism. 27 (3.8%) of the all patients had prior partial thyroidectomy history. Of 149 patients who had thyroid scintigraphy; 47 (31.5%) had hyperactive, 55 (37%) had hypoactive, 47 (31.5%) had both hypo and hyperactive nodules.

67 of 719 patients were performed twice UG-FNAB, 5 of them were performed 3 times. UG-FNAB repeated in 52 patients due to prior non-diagnostic cytology, in 10 patients for routine follow up and in 5 patients for prior atypia of undetermined significance. Some patients even underwent three times UG-FNAB due to prior non-diagnostic cytology.

The results of 790 UG-FNAB of 719 patients were as follows: 567 (71.77%) benign cytology, 97 (12.28%) non-diagnostic cytology, 43 (5.44%) atypia of undetermined significance, 81 (10.25%) suspicious for malignancy and 2 (0.25%) malignant.

606 (84.2%) of the patients were underwent clinical follow-up. Total thyroidectomy was offered to 95 (13.2%) patients, due to suspicious UG-FNAB cytology or clinical suspicion for malignancy or multinodular goitre. Of 17 (2.4%) patients were given radioactive iodine therapy for thyrotoxycosis. The patients whom we have offered to total thyroidectomy, 60 of them were underwent thyroid surgery at our hospital whereas 35 of them were lost to follow up. Postoperative histopathological examination of 60 thyroid glands specimens have showed that 51 (85%) of them had nodular goitre; whereas 3 (5%) of had follicular adenoma, and 6 (%15) of them had thyroid papillar carcinoma.

Demographic and nodular features of the patients were summarized at Table 1. If we compared to ultrasonographic features of the benign and malign nodules proven by total thyroidectomy; no features were found to be significantly different between benign and malign nodules (Table 1).

Morphological and clinical features of 60 patients who underwent total thyroidectomy were shown at Table 2. The overall differentiated thyroid carcinoma ratio (confirmed by postoperative histopathological examination) was 0.84% for 719 patients. All of our nodules (n=6) which reported as “malignant” did not exceed 3 cm in diameter.

If we focuse on 6 thyroid papillar carcinoma cases which were detected after total thyroidectomy; 2 of them were already determined as “malignant” by UG-FNAB at first biopsy. Four of them had a malignant tumor greater than 1 cm, whereas 2 of them were < 1cm. Patient who had micropapillar thyroid carcinoma was 49 years old male. He had multinodular goitre. Tumor diameter was 0.8 cm and maximum nodule diameter was also 0.9 cm. And he had also had a follicular adenoma at another thyroid nodule < 1 cm at the other side of thyroid gland. Similarly, 71 years old female had a tumor in one of her thyroid nodules, and also had a follicular adenoma at another thyroid nodule < 1 cm. Four of the papillar carsinoma cases were

detected by malignant or suspicious cytology at their first UG-FNAB. But in 2 patients UG-FNAB had to be repeated because of prior non-diagnostic cytology.

If we analyze the subgroup of 308 nodules which were equal or greater than 1 cm, number of thyroid carsinoma cases were 4 (1.3%).

Table 1: Nodular features of 719 patients		Benign (n= 713)	Malign (n=6)	p
Age		51.55±13.8 (16-90)	55.5±16 (39-79)	0.996
Gender	Male	102	1	0.314
	Female	611	5	
Thyroid function tests	Euthyroid	503	4	0.985
	Hyperthyroidism	104	2	
	Hypothyroidism	110	0	
Number of nodules	one	291	4	0.765
	two	49	0	
	More than two	373	2	
Diameter of the nodules	<1cm	405	2	0.658
	1 cm	53	1	
	> 1cm	255	3	
Echogenity	Hypoechoic	604	5	0.809
	Isoechoic	82	1	
	Hyperechoic	33	0	
Margin of the nodules	irregular	18	1	0.685
	regular	695	5	
Macrocalcification	absent	606	6	0.910
	present	107	0	
Microcalcification	absent	702	5	0.759
	present	11	1	
Nature of nodules	solid	271	3	0.322
	cystic	61	0	
	mixt	281	3	

Table 2: Features of 60 patients whom underwent thyroid surgery in our hospital.

Total thyroidectomy (n=60)		Benign (n=54)	Malign (n=6)	p
Age		51±11.9 (25-73)	55.5±16 (39-79)	0.513
Gender	Male	12	1	0.754
	Female	42	5	
Thyroid function tests	Euthyroid	23	4	0.088
	Hyperthyroidism	7	2	
	Hypothyroidism	24	0	
Number of nodules	one	17	4	0.227
	two	1	0	
	More than two	36	2	
Diameter of the nodules	<1cm	36	2	0.242
	1 cm	3	1	
	> 1cm	15	3	
Echogenity	Hypoechoic	46	5	0.832
	Isoechoic	6	1	
	Hyperechoic	2	0	
Margin of the nodules	irregular	2	1	0.167
	regular	52	5	
Macrocalcification	absent	42	6	0.197
	present	12	0	
Microcalcification	absent	53	5	0.550
	present	1	1	
Nature of nodules	solid	20	3	0.569
	cystic	8	0	
	mixt	26	3	

Table 3: Features of 6 thyroid malignancy proven by total thyroidectomy.

No	1	2	3	4	5	6
Age	49	71	39	79	42	53
Gender	M	F	F	F	F	F
TFT	Hyperthyroid	Hyperthyroid	Euthyroid	Euthyroid	Euthyroid	Euthyroid
Number of the Nodules	More than 2	More than 2	1	1	1	1
Diameter	< 1 cm	1 cm	< 1 cm	>1 cm	>1 cm	>1 cm
Echogenity	Hypoechoic	Hypoechoic	Isoechoic	Hypoechoic	Hypoechoic	Hypoechoic
Margine	Regular	Regular	Regular	Irregular	Regular	Regular
Nature	Solid	Solid and cystic	Solid	Solid and cystic	Solid	Solid
Calicifications	None	Macrocalcifications	None	None	None	None
Scintigraphic features	Hypo and hyper active	Hypoactive	-	-	Hypo and hyper active	-
1st UG-FNAB	SM	ND	M	M	ND	AUS
2nd UG-FNAB	-	SM	-	-	SM	-

SM: Suspicious for malignancy , ND: Non-diagnostic, AUS: atypia of undetermined significance, M: Malignant.

Discussion

Although thyroid nodular disease is common, only a small number of thyroid nodules are malignant. UG-FNAB plays an important role in differentiating benign thyroid nodules from malignant nodules. It is essential to identify which thyroid nodules require UG-FNAB. The recent guidelines were published by The American Thyroid Association (ATA) in 2009 [8]. The American Association of Clinical Endocrinologists (AACE), the Italian Association of Medical Endocrinologists (AME), and European Thyroid Association (ETA) published new in guidelines in 2010, and then a revision was made in 2011 [9,10]. ATA guidelines recommend UG-FNAB in all suspicious nodules > 5 mm (grade A recommendation) [8]. The ETA and AACE guidelines also recommend UG-FNAB, that nodules < 1cm if the clinical and/or ultrasonographic suspicious is present [9,10]. Atypical UG-FNAB results should be interpreted in the context of the clinical presentation of thyroid nodular disease, imaging data, and the presence of risk factors

for malignancy, including patient age, sex, ethnic background, exposure to ionizing radiation, and familial history of thyroid malignancy [9,11]. Recent literature indicates that patients with multiple thyroid nodules have the same risk of malignancy as patients with solitary thyroid nodules [12,13]. Ultrasonographic characteristics are more reliable indicators of potential malignancy than nodule size [14-16].

On histopathological examination of various FNAB specimens, 5-20% of them are reported to be insufficient or non-diagnostic [17-20]. Compatible with current data, in our study, non-diagnostic cytology were reported to be as 12.28%.

Instead of UG-FNAB, ultrasonographic monitoring is preferred in thyroid nodules which have diameter less than 5 mm, because of the difficulties to reach the nodule and the risk of obtaining inadequate material. In our study the nodules which surgery were performed with diameter of < 10 mm, and ≥ 5 mm, 2 micropapillar carcinoma was detected. On cytopathological examination of their FNAB, one of them was reported to be suspicious for malignancy, other was malignant. None of them have any calcifications on their ultrasonographic examinations. Both of them also had a follicular adenoma at another thyroid nodule < 1 cm. (Table 3).

In our study, thyroid carcinoma rate was found to be lesser than in current literature. One of the reason for this may be higher ratio of nodules that underwent evaluation were lesser than 1 cm in diameters. But if we analyze the subgroup of the nodules equal to or greater than 1 cm, papillar carcinoma rate was still lesser (1.3%). There was no significance between the groups which have nodule < 1cm, and ≥ 1 cm ($p>0.05$). Our results may indicate that our region were associated with lesser papillar carcinoma rate. If we compere our results with some studies which were performed in our country, similar cytological malignancy rates could be seen [21-24].

Sengoz et al. were reported UG-FNAB cytological results as 781 (84.1%) benign, 35 (3.8%) malignant suspicious, 21 (2.3%) malignant nodules and 92 (9.9%) inadequate materials [21]. Similarly with ours, this malignancy rates were also lesser than current literature. In another

study including 1420 patients; 30 (3.7%) malignant suspicious, 8 (0.9%) malignant nodules were reported, in 808 cytological findings of FNAB specimens [22]. By histopatological examination of l52 surgical specimens after thyroid operation, 35 of them were diagnosed as thyroid carcinoma. If we thought that, we have already had UG-FNAB cytology reports of 808, before the thyroid surgery; we could conclude that their malignancy rate proven by surgery was 4.3% (n=808) [22]. In another Turkish study, 197 cases who had been diagnosed as multinodular goitre were analyzed. After 26 inadequate cytological results were excluded, 171 specimens were examined. In a group of dominant nodules, malignancy and suspicious for malignancy rates were 1.8% and 9.4% whereas they were 0.6% and 11.1%, respectively. In this study, dominant and non-dominant nodule diameters were determined as 24.96±9.08, and 15.4±5.89 mm. If we thought that, nodule diameters in our study were lesser than 30 mm, lesser malignancy rates in our study could explained by having smaller nodule diameters [23]. In another study, one group (group A), consisted of thyroid nodules which had ultrasonographically suspicious criteria for malignancy, the other group (group B) which were not ultrasonographically suspicious for malignancy but referred to biopsy according to clinicians view. FNAB cytologies were as follows: In group A; 28 (50.9%) benign, 16 (29.1%) malign, 8 (14.5%) suspicious for malignancy, and 3 (5.5%) inadequate material. In group B; 74 (96.1%) benign, 1 (1.3%) malign, 1 (1.3%) suspicious for malignancy, and 1 (1.3%) inadequate material [24]. If we focuse on our malignancy results in nodules > 1 cm, this result is similar to ours. By being the one center which could perform UG-FNAB, other clinicians had been directed patients with thyroid nodule to our outpatient clinic. So, because of that, our indications for UG-FNAB might be higher than already needed. We thought that, thyroid cancer risk could be detected by using UG-FNAB even in thyroid nodules smaller than 1 cm, if the nodule has sonographically suspicious features for malignancy. So, it requires stronger collaboration between radiologist and endocrinologist.

In conclusion, fine needle aspiration biopsy is a functional and reliable diagnosing method. Using UG-FNAB leads to identify discrete nodules and direct needle localization and provides adequate specimen. UG-FNAB has become a predominant method for the diagnosis of benign and malign thyroid nodules. Atypical UG-FNAB results need to be considered in combination with clinical presentation, imaging data, and individual risk factors. Collaboration between endocrinologists, radiologists and pathologists is essential for patients with thyroid nodules to avoid missestimation of the risk of thyroid cancer.

Conflict of interest: None.

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