

Original Article

Fine needle aspiration biopsy of thyroid nodules: cytologic and histopathologic correlation of 1096 patients

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Abstract: Via routinely used thyroid function tests, scintigraphy and ultrasonography (USG), important information is obtained in the clinical and diagnostic practice for thyroid nodules. However, the distinction between benign and malignant lesions cannot precisely be performed with these tests. Thyroid fine needle aspiration biopsy (FNAB) is considered the most reliable diagnostic method in the differentiation between benign and malignant thyroid nodules. It has recently been likely to perform aspiration from deeper nodules via the implementation of FNAB along with USG. Today, in cytopathological examination of thyroid FNAB, standardized Bethesda System for Reporting Thyroid Cytopathology (BSRTC) system is used. Here, FNAB was performed in 1096 patients with thyroid nodules in the Medical School of Selcuk University between January 2009 and July 2014. Patients consisted of 919 women and 177 men between 12 and 87 years of age. Evaluated via BSRTC, the results were classified as unsatisfactory, benign, atypia (or follicular lesions) of undetermined significance (AUS), follicular neoplasm or lesions suspicious for follicular neoplasm (FN), suspected malignant and malignant. After FNAB, 183 patients were operated and evaluated histopathologically. Histological malignancy rates of the categories were as follows: 16% (5), 15% (6) 14% (1) 60% (9), 72% (18) and 97% (63), respectively. In our study, we aimed to compare FNAB results of thyroid nodules with histopathology results after thyroidectomy and to show the sensitivity and specificity of FNAB technique to be higher in the follow-up and diagnosis of thyroid lesions. Given the malignancy detection rate in the follow-up of patients whose cytology was reported as inadequate, we also consider follow-ups are important in these patients.

Keywords: Thyroid, fine needle aspiration biopsy, bethesda

Introduction

As in the whole world, thyroid diseases are also considered to be one of the common diseases in our country, Turkey. Thyroid nodules are seen between 4-7% in the general population, and 5-10% of these cases are malignant [1, 2]. Low as the rate seems, the early diagnosis of these cancers is very important because of their slow progression and patients' longevity due to early treatment [3, 4]. For cytological interpretation, fine-needle aspiration biopsy (FNAB) is an established diagnostic modality in the evaluation of thyroid nodules. Although nearly 75% of these modalities definitively produce benign or malignant diagnoses, and the accuracy of those diagnoses exceeds 95%, indeterminate or suspicious results are frequent and challenging in terms of defining an appropriate management strategy. While standardized Bethesda System for Reporting Thyroid Cytopathology

(BSRTC) system has brought standardization to the diagnostic terminology of thyroid cytology, morphological interpretation still remains as an inherently subjective practice that leads to interobserver discrepancies [5-7].

Because FNAB results are reliable, cost effective, well tolerated by patients and cause very few complications, FNAB is the first choice in the diagnosis of thyroid nodules [8-10]. In our study, we aimed at comparing the cytological results of patients exposed to FNAB due to thyroid nodules with the histopathological findings of surgical specimens, and at determining the sensitivity and specificity of FNAB.

Materials and methods

In our study, the patients admitted to the general surgery and otolaryngology departments of the university hospital of The Medical School of

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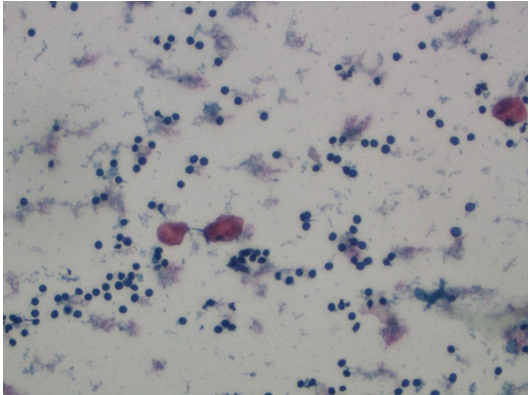


Figure 1. Benign cytology (PAP, ×400).

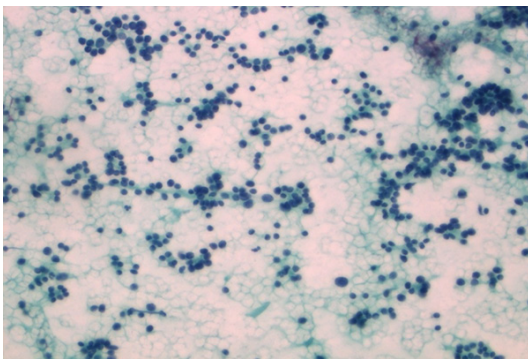


Figure 2. Follicular Neoplasia (PAP, ×400).

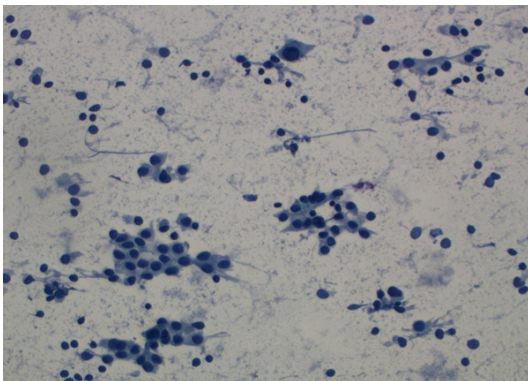


Figure 3. Malignant cytology (PAP, ×400).

Selcuk University between January 2009 and July 2014 and exposed to FNAB due to suspected nodular goitre, multinodular goitre, hyperthyroidy and throid cancer and then to surgery were retrospectively investigated. Of 1096 patients constituting the study population, 919 were women, and 177 were men between 12-87 years of age (average 49.5 years). All patients were exposed to FNAB. Cytological specimens were stained with the dyes of Papa-

nikolaou (PAP), May-Grünwald Giemsa (MGG) and Hematoksilen-Eozin (HE). In histopathological evaluation performed via BSRTC, the results were classified as unsatisfactory, benign, atypia (or follicular lesions) of undetermined significance (AUS), follicular neoplasm or lesions suspicious for follicular neoplasm (FN), suspected malignant and malignant.

Cellular adequacy was considered insufficient, less than optimal or adequate. Insufficient cases had no atypical findings and fewer than 6 groups of 10 benign follicular cells [5].

Results

Among 1096 specimens of FNAB, 12% (132) were reported as unsatisfactory, 72% (789) as benign (**Figure 1**), 3% (29) as atypia (or follicular lesions) of undetermined significance (AUS), 3% (35) as follicular neoplasm or lesions suspicious for follicular neoplasm (FN) (**Figure 2**), 4% (46) as suspected malignant and 6% (65) as malignant (**Figure 3**). The gender and age distributions of the patients diagnosed cytologically are presented in **Tables 1** and **2**. The specimens of 183 patients operated after FNAB were histopathologically evaluated, and the malignancy rates in these categories were determined as follows: 16% (5), 15% (6), 14% (1), 60% (9), 72% (18) and 97% (63), respectively. The age distributions of 102 patients (77 women and 25 men) determined as histologically malignant were 11 between 0-30 years, 68 between 31-60 and 23 over 60. The cytological and histological correlations of these patients are presented in **Table 3**.

Those with unsatisfactory FNAB cytology of thyroid nodules were excluded out of the criteria. In our comparison, those reported as the suspected were included into the malignancy group. The sensitivity and specivity of preoperative thyroid FNAB on postoperative diagnosis, and the negative and positive predictive values were investigated. The rates of validity, sensitivity, specificity, positive predictive and negative predictive values in our study were detected as 88%, 93%, 79%, 90% and 85%, respectively.

Discussion

Thyroid nodules are among commonly encountered endocrine pathologies. In western countries, the rate of thyroid nodules detected palpably ranges between 3-8% [11]. In Turkey, the prevalence of thyroid nodules was determined

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Table 1. Cytologic diagnosis sex distribution

Sex	Total	Inadequate	Benign	Atypia of undetermined significance	Follicular Neoplasm/Suspicion	Suspicion of malignancy	Malignant
Women	919	110	671	25	27	38	48
Men	177	22	118	4	8	8	17

Table 2. Age distribution of cytological diagnosis

Age	Total	Inadequate	Benign	Atypia of undetermined significance	Follicular Neoplasm/Suspicion	Suspicion of malignancy	Malignant
0-30	86	21	44	2	8	7	4
31-60	773	81	571	21	24	28	48
>60	237	30	174	6	3	11	13
Total	1096	132	789	29	35	46	65

Table 3. Cytologic-histologic correlation

Cytological diagnosis	Number of patients operated with	Benign	Papillary Carcinoma	Follicular carcinoma	Medullary Carcinoma
Inadequate	31	26	5	0	0
Benign	40	34	5	1	0
AUS	7	6	1	0	0
FN	15	6	4	4	1
Suspicion of malignancy	25	7	18	0	0
Malignant	65	2	63	0	0

as 2-6% with palpable examination and 18% with ultrasonography (USG) [12, 13]. Thyroid cancers consist of 1% of all malignant neoplasms and are seen three or four times more frequently in women, compared to men. In our study, as to the detection of thyroid malignancy, the rate was women/men: 77/25=3.08, and our rate is consistent with that reported in literature [14]. Age and gender are definitive criteria in terms of the malignancy of nodules. While the likeliness of nodules to be observed as malignant in women between the ages of 20-40 is lower, this rate increases in nodules witnessed in men at advanced ages. Although the likeliness of malignancy was increased in both genders with advanced age in our study, no significant association was determined between malignancy, and gender and age.

Upon the diagnosis of thyroid nodules, the main problem is to distinguish between whether nodules are benign or malignant. FNAB is known to be the most accurate and cost-effective test in order to evaluate thyroid nodules [15]. The malignant and benign diagnoses performed by pathologists are easily understood and managed by clinicians. However, indetermi-

nate diagnoses may cause confusion and uncertainty of the management among patients and clinicians [16]. BSRTC provides a consensus in diagnostic terminology and morphological criteria for pathologists, related to implied risks of malignancy and recommendations in patient management [17-20]. In literature, the rate of malignancy was reported as 80-90% for papillary carcinomas, as 5-15% for follicular carcinomas, as 3-5% for medullary carcinomas, as 0.4-10% for hürthle cell carcinomas, as 1-3% for anaplastic carcinomas and as 1-2% for other malignancies [21, 22]. In our study, of 102 malignant cases, 96 (94%) were detected to be papillary carcinomas, 5 (5%) to be follicular carcinomas, and only one (1%) to be medullary carcinomas. While papillary carcinomas are encountered a little more frequently, the distribution of these cancers was consistent with that reported in other studies, and no anaplastic carcinomas, seen less than other types, were encountered in our study.

It may sometimes be impossible to diagnose cytologically medullary thyroid carcinomas with more aggressive nature. In a meta-analysis study, it was reported that while 56% of histo-

logically proven medullary thyroid carcinomas were correctly detected by cytologic evaluation, the remaining medullary thyroid carcinomas were defined as benign, indeterminate, nondiagnostic or as other types of neoplasms by FNAB [23].

In our study, of 46 cases where FNAB results were evaluated as suspected malignant, 25 were operated on, and 18 were determined with malignancy. Due to risk of malignancy, surgery is recommended for the certainty of diagnosis in cases with suspected malignancy [24].

The target of FN category is to determine nodules that may be follicular carcinoma and to triage them for surgical lobectomy. Based on BSRTC, 15-30% of cases classified as FN prove to be malignant [17, 25]. Among 15 patients whose FNABs were indicated as follicular neoplasms in our study, surgical pathology findings of nine cases were reported as malignant. We consider that the patients reported as follicular neoplasms should be operated on [26].

In our study, of 35 (3%) patients in AUS category, only one (14%) was determined as malignant. According to BSRTC, the rate of AUS interpretations in a laboratory should range between 3 and 6% of all thyroid FNABs, and should not be over 7%, because higher rates most probably represent an overuse of this category, and other interpretations may be more appropriate [17, 27-30].

The rate of unsatisfactory materials in FNAB reported in literature ranges between 10% and 28.2%. This rate, however, was found as 12% in our study. In previous studies, the reasons decreasing the productivity of FNAB were reported as unsatisfactory sampling, unexperienced cytopathologists and difficulty in distinguishing between follicular lesions. Because the follicular variants of hyperplastic adenomatoid nodules, follicular adenomas, well-differentiated follicular carcinomas and papillary carcinomas are of similar criteria to each other, it is difficult to differentiate between these lesions via FNAB [31]. In order to achieve FNAB of thyroids, providing satisfactory specimens and existence of experienced cytopathologists are two important factors. Patients with unsatisfactory specimens should undergo repeated FNAB, preferably under sonographic guidance [13, 32]. The current study demonstrated that among patients with initial unsatisfactory specimens ex-

posed to repeated thyroid FNAB, 83% had a diagnostic repeated FNAB allowing appropriate follow-ups. The malignancy rate (8.5%) in repeated FNABs because of prior unsatisfactory aspiration was comparable to the malignancy rate for the patients with a diagnostic initial FNAB (7.6%) [33].

In conclusion, the sensitivity and specificity rates of FNAB used as the first step modality in the evaluation of thyroid nodules were reported to change between 65-99%, 72-100% and 76-100% in literature, respectively [10, 14, 34]. Given that the cytology of suspected FNABs were accepted as malignant in our study, the sensitivity and specificity rates were found as 93% and 79%, as consistent with the findings given in literature.

In summary, our study demonstrated that thyroid FNAB is an accurate and relatively precise tool in the diagnosis of thyroid malignancy. Six diagnostic categories of thyroid cytology are very useful for triaging patients with thyroid nodules for clinical management [33, 35, 36]. Additionally, considering that the rate of malignancy was determined as 16% in the follow-ups of patients reported as unsatisfactory, the importance of repeating FNABs is quite remarkable.

Disclosure of conflict of interest

None.

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