Tiroid Nodüllerinin Değerlendirilmesinde Bethesda Sistemi ve İnce İğne Aspirasyon Biyopsisinin Yeri

The Role of Fine Needle Aspiration Biopsy with Bethesda System in the Evaluation of Thyroid Nodules

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Abstract

Aim: In this study, the role of fine needle aspiration biopsy (FNAB) evaluated with the Bethesda System in the diagnosis of thyroid nodules was investigated.

Materials and Methods: Total 2284 FNAB materials of 1846 patients were performed in the Pathology Department of Kutahya Health Sciences University, Evliya Celebi Traning and Research Hospital between 2016 and 2019 and reported according to the Bethesda category. Among these cases, diagnostic sensitivity, specificity, accuracy, positive and negative predictive values of FNAB were calculated by making cyto-histopathological comparison in 328 cases who underwent total thyroidectomy.

Results: In the study, 1538 of the 1846 patients included were female (83.31%) and 308 (16.68%) were male. The average age was 49.92 years (Age range 19-87). The final cytological diagnoses of 2284 FNABs were as follows: 287 (12.57%) nondiagnostic or unsatisfactory, 1517 (66.42%) benign cytology, 316 (13.83%) atypia of undetermined significance/follicular lesion of undetermined significance, 63 (2.75%) follicular neoplasm or suspicious for a follicular neoplasm, 59 (2.59%) suspicious for malignancy and 42 (1.84%) malignant cytology. Histologically, 245 (74.70%) of the 328 cases were benign, while 83 (25.30%) were malignant. The number of true negative cases was 216 (65.85%), the number of true positive cases was 62 (19.90%), the number of false positive cases was 29 (8.84%) and the number of false negative cases was 21 (6.40%). In this case, diagnostic sensitivity, specificity, accuracy rates, positive and negative predictive values were 74.7%, 88.16%, 84.76%, 68.13% and 91.14%, respectively.

Conclusion: In our study, it was observed that the sensitivity, specificity, accuracy rates, positive and negative predictive values of thyroid FNABs were compatible with the literature. We think that as the experience of the clinician and cytopathologist increases, false negative and positive results will decrease and at the same time, the confidence in thyroid FNABs will increase even more with the participation of some recent molecular methods (BRAF, RET/PTC, PAX8/PPARG and RAS) applied to FNABs.

Keywords: Bethesda system; fine needle aspiration biopsy; thyroid nodule; cytology

Öz

Amaç: Bu çalışmada tiroid nodüllerinin tanısında Bethesda Sistemi ile değerlendirilen ince iğne aspirasyon biyopsisinin (İİAB) rolü araştırıldı.

Gereç ve Yöntemler: Kütahya Sağlık Bilimleri Üniversitesi Evliya Çelebi Eğitim ve Araştırma Hastanesi Patoloji Bölümü'nde 2016-2019 yılları arasında Bethesda kategorisine göre raporlanan 1846 hastaya ait 2284 İİAB materyali incelendi. Bu olgular içerisinden tiroidektomisi yapılan 328 olguda sito-histopatolojik karşılaştırma yapılarak İİAB'nin tanısal duyarlılık, özgüllük, doğruluk, pozitif ve negatif prediktif değerleri araştırıldı.

Bulgular: Çalışmaya alınan 1846 hastanın 1538'i kadın (%83,31), 308'i (%16,68) erkekti. Yaş ortalaması 49,92 idi (Yaş aralığı 19-87). 2284 İİAB'nin son sitolojik tanıları şöyleydi: 287 (%12,57) yetersiz materyal, 1517 (%66,42) benign sitoloji, 316 (%13,83) önemi belirsiz atipi/önemi belirsiz foliküler lezyon, 63 (%2,75) foliküler neoplazi veya foliküler neoplazi kuşkusu, 59 (%2,59) malignite kuşkulu sitoloji ve 42 (%1,84) malign sitoloji. Histolojik olarak toplam 328 olgunun 245'i (%74,70) benign iken, 83'ü (%25,30) maligndi. Gerçek negatif olgu sayısı 216 (%65,85), gerçek pozitif olgu sayısı 62 (%19,90), yalancı pozitif olgu sayısı 29 (%8,84), yalancı negatif olgu sayısı 21 (%6,40) bulundu. Bu durumda tanısal duyarlılık, özgüllük, doğruluk oranları, pozitif ve negatif prediktif değerleri sırasıyla %74,7, %88,16, %84,76, %68,13 ve %91,14 olarak saptandı.

Sonuç: Çalışmamızda tiroid İİAB'lerindeki duyarlılık, özgüllük, doğruluk oranları ile pozitif ve negatif prediktif değerlerinin literatürle uyumlu olduğu görüldü. Klinisyen ve sitopatoloğun deneyimi arttıkça, yalancı negatif ve pozitif sonuçların azalacağı ve aynı zamanda İİAB'lere uygulanan bazı yeni moleküler yöntemlerin de (BRAF, RET/PTC, PAX8/PPARG ve RAS) katılımıyla, tiroid İİAB'lerine olan güvenin daha da artacağını düşünmekteyiz.

Anahtar Sözcükler: Bethesda sistemi; ince iğne aspirasyon biyopsisi; tiroid nodülü; sitoloji

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INTRODUCTION

Fine needle aspiration biopsy (FNAB) is an effective and reliable method in the evaluation of thyroid nodules and is considered the gold standard for preoperative evaluation (1-3). FNAB is an inexpensive, easy-to-apply method with a low risk of complications that prevents unnecessary surgical intervention by helping to determine the diagnosis before surgery (1-3). Bethesda reporting system was defined by the National Cancer Institute in Bethesda, USA, in 2007 in the evaluation of thyroid FNAB materials. With the use of this system since 2009, standardization has been achieved with the categorization in the diagnosis, and the harmony and understanding between pathologist and clinician in patient management has increased.

Today, the Bethesda System, which has 6 diagnostic categories for thyroid cytology reporting, is widely used in the evaluation of thyroid FNA materials. These categories are nondiagnostic (ND) or unsatisfactory (UNS), benign cytology (BC); atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS), follicular neoplasm (FN) or suspicious for a follicular neoplasm (SFN), suspicious for malignancy (SM) and malignant cytology (MC) (4,5).

In this study, our FNAB results performed using the Bethesda reporting system in our center were retrospectively analyzed and its effectiveness was evaluated by comparing its compatibility with the literature.

MATERIALS AND METHODS

Ethics committee approval was obtained from the Clinical Research Ethics Committee of Kutahya University of Health Sciences for our study (Date: 27/06/2019, Decision No: 2019/07-2). Cytological examination results of 2284 materials of 1846 patients who underwent thyroid FNAB were retrieved from the files in the Pathology Department of Kutahya Health Sciences University Evliya Celebi Traning and Research Hospital for a period of 3 years (2016-2019). Cytological and histopathological diagnoses were compared in 328 patients who underwent total thyroidectomy. Pathological evaluation was made by 5 different pathologists. Only past pathology reports were evaluated without cross-comparisons between diagnoses.

Patients with thyroid FNAB diagnosed as ND or UNS (Bethesda class I), were not included in the study. Only 328 cases who had both total thyroidectomy and FNAB and had the chance to compare histology-cytology diagnoses were included in the study.

Cytological results were divided into two main groups: Patients diagnosed with BC and AUS/FLUS in cytology were considered as benign groups, while cases with FN/SFN, SM and MC were considered as malignant groups. Cytologically diagnosed as FN/SFN, SM and MC (malignant group), histopathologically malignant cases were considered true positive; cytologically diagnosed as BC and AUS/FLUS (benign group) and histopathologically diagnosed benign cases were considered true negative; cytologically diagnosed cases of FN/SFN, SM and MC (malignant group) but histopathologically benign cases were considered false positive; cytologically diagnosed BC and AUS/FLUS (benign group) but histopathologically malignant cases were considered false negative.

The diagnostic sensitivity, specificity, accuracy, positive likelihood ratio, negative likelihood ratio, positive predictive value and negative predictive value ratios were calculated with these data according to the method of Galen and Gambino (Table 1). Patients with nondiagnostic FNAC were excluded from the calculations.

RESULTS

Of the 1846 patients included in the study, 1538 were female (83.31%) and 308 (16.68%) were male. The average age was 49.92 (Age range 19-87). Malignancy rates of our cases, cytological diagnoses according to the by the Bethesda System for Reporting Thyroid Cytopathology categories comparison with the literature are summarized in Table 2.

Of 328 cases who underwent thyroidectomy, 236 (71.95%) were female and 92 (28.04%) were male. The mean age of the patients was 48.83 and the age range was 22-78. According to histopathological diagnosis, 245 of the cases were benign (74.70%) and 83 of them were malignant (25.30%). Table 3 shows details in comparison with our fine needle aspiration biopsy and histopathological results.

The number of false positive cases were 29 in total and the distribution of false positive cases were as

Table 1. Methods of Galen and Gambino

Sensitivity	GP/GP+FN
Specificity	GN/GN+FP
Accuracy	TP+TN/TP+TN+FP+FN
Positive likelihood ratio	Sensitivity/(1-Specificity)
Negative likelihood ratio	(1–Sensitivity)/Specificity
Positive predictive value	TP/TP+FP
Negative predictive value	FN/FN+TN

TP=True Positive, TN=True Negative, FP=False Positive, FN=False Negative

follows: 19 FN/SFN [11 nodular goiter (NG) + 8 follicular adenoma (FA)], 9 SM [3 NG+1 subacute thyroiditis (SAT)+2 hashimoto thyroiditis (HT)+1 FA +2 hurthle cell adenoma (HHA)] and 1 MC (1 HT). The number of false negative cases were 21 in total and the distribution of false negative cases were as follows: 10 BC [(2 thyroid papillary carcinoma (PTC)+8 papillary thyroid microcarcinoma (PTMC)] and 11 AUS/FLUS (4 PTC and 7 PTMC). According to the cytology-histopathology comparison; the number of true negative cases were 216 (65.85%), the number of true positive cases were 62 (19.90%), the number of false positive cases were 29 (8.84%), the number of false negative cases were 21 (6.40%) (Table 4).

In this case, sensitivity, specificity and accuracy rates were 74.7%, 88.16% and 84.76%, respectively. The positive likelihood ratio was 6.31, the negative likelihood ratio was 0.29, the positive predictive value was 68.13%, the negative predictive value was 91.14%.

DISCUSSION

Cytological analysis of FNAB specimens is used to estimate malignancy risk and the most appropriate cytological classification of malignancy risk is the Bethesda system for thyroid cytopathology.

According to the Bethesda reporting system used in the classification of FNAB materials, ND or UNS (Bethesda class I), is seen between 2-20%, while its ideal is below 10% (4,5). The current study, this rate was 12.56%. The BC category accounts for 60-70%, and the malignancy rate is between 0-3% of all cases (4,5). The current study, BC rate was 66.42% and malignancy rate was 0.65%, and was consistent with the literature. According to the Bethesda reporting system the rate of diagnosis of AUS/FLUS is between 3-6% and the risk of malignancy in this group is between 10-30% (4,5). In a study of 26 cases of AUS/FLUS were randomly selected and reevaluated blindly by 2 experienced reviewers (1). Unanimous interobserver and intraobserver agreement was observed in only 60% of cases (1). This demonstrated that although both professionals used same diagnostic criteria, these individuals had various thresholds for applying these criteria (1). However, to maintain its usefulness, the proportion of AUS/FLUS should be used as little as possible (1). The current study, the rate of diagnosis of AUS/FLUS was 13.83%, and it was higher than the literature while the rate of malignancy detected in this group was 4.43%, which was lower than the literature (4,5). It was thought that the reason for the low rate of malignancy found in this group in current study compared to the literature might be due to the high rate of AUS /FLUS diagnosis percentage. Malignant lesions occur in 25-40% of the FN/SFN group (4,5). The current study, this rate was 22.22% and it was slightly lower than the literature (4,5). The rate of malignancy risk in the SM group varies between 50-75%, and the current study, this rate is 30.5% and is lower than the literature (4,5). Malign cytology accounts for 3-7% of all FNABs, it is 97-99% malignant and most of them are PTC (4,5). The current study, the percentage of MC was 1.84%, of which 69.50% were malignant and 55.17% of them were PTC and 34.53% of them were PTMC (Table 4). The reason of the low percentage of the malignancy in excision materials was the low excision percentage of the cases diagnosed with malignant group in FNAB. Excised FNAB rates were 33/63 (52.38%) in the FN/SFN group, 28/59 (47.45%) in the SM group, and 30/42 (71.42%) in the MC group.

Papillary thyroid carcinoma is the most common thyroid malignancy and constitutes 70-80 % of all thyroid malignancies (6). The current study, 95.18 % of the malignancies detected were PTC, and the majority of them were PTMCs (64.55 %). In addition, 3 (3.61%) were follicular carcinoma (FC) and 1 (1.20 %) were hurthle cell carcinoma (HCC). It is 3-4 times more common in women than in men (6). The current study, the female/male ratio is 3.2 in terms of frequency of malignancy, and it seems to be compatible with the literature (6).

Table 2. Case number and frequency of 2284 thyroid fine needle aspiration cytology by The Bethesda System for Reporting Thyroid Cytopathology categories comparison with the literatüre (3,4)

Bethesda category	Case number of our study	Case frequency of our study	Case frequency of the literatüre	Malignancy frequency of our study	Malignancy frequency of the literature
I- ND / UNS	287	12.56%	2-20%	-	5-10%
II- BC	1517	66.42%	60-70%	0.65%	0-3%
III- AUS / FLUS	316	13.83%	3-6%	4.43%	10-30%
IV- FN / SFN	63	2.75%	2-25%	22.22%	25-40%
V- SM	59	2.59%	1-6%	30.50%	50-75%
VI- MC	42	1.84%	3-7%	69.50%	97-99%
Total	2284	100%			

ND: Nondiagnostic, UNS: Unsatisfactory, BC: Benign cytology, AUS: Atypia of undetermined significance, FLUS: Follicular lesion of undetermined significance, FN: Follicular neoplasm, SFN: Suspicious for a follicular neoplasm, SM: Suspicious for malignancy, MC: malignant cytology

Table 3. In comparison with our fine needle aspiration biopsy and histopathological results

		Histopathological results											
		Benign (n=245)						**Malignant (n=83)**					
		Total case number	NG	SAT	HT	FA	HCA	PTC (n=28)		PTMC (n=51)		FC (n=3)	HCC (n=1)
								FV	KV	FV	KV		
FNAB Results	BC	194	148	-	12	24	-	2	-	2	6	-	
	AUS / FLUS	43	7	-	6	15	4	3	1	4	3	-	
	FN / SFN	33	11	-	-	8	-	2	1	3	4	3	1
	SM	28	3	1	2	1	2	2	1	4	12	-	
	MC	30	-	-	1		-	6	10	4	9	-	
	Total	328	169	1	21	48	6	15	13	17	34	3	1

BC: Benign cytology, AUS: Atypia of undetermined significance, FLUS: Follicular lesion of undetermined significance, FN: Follicular neoplasm, SFN: Suspicious for a follicular neoplasm, SM: Suspicious for malignancy, MC: malignant cytology.
NG: Nodular goiter, SAT: Subacute thyroiditis, HT: Hashimoto thyroiditis, FA: Follicular adenoma, HCA: Hurthle cell adenoma, PTC: Papillary thyroid carcinoma, PTMC: Papillary thyroid microcarcinoma, FV: Follicular variant, CV: Classic variant, FC: Follicular carcinoma, HCC: Hurthle cell carcinoma

In the literature, FNAB sensitivity ranges from 57-99%, and specificity ranges from 60-99 (2,3,7-14). When calculating the sensitivity and sensitivity, what needs to be done is to divide the cytological and histopathological diagnoses into 2 groups as malignant and benign. This distinction is not so clear especially in the Bethesda classification, which has 6 diagnostic categories and is used in cytological evaluation. The reason why the sensitivity and specificity are in such a wide range in the literature is due to the difficulty and differences in identifying benign and malignant groups in studies (2,3,7-14). In our study, as in most of the studies, the FN/SFN category was accepted in the malignant group in addition to the MC category. In the study of Önver et al., when only MC patients were considered as malignant group, FNAB sensitivity, specificity and accuracy rate were 90.7%, 40%, 100%, respectively, while this rate decreased to 73.9%, 77.4% and 76.5% when SM and MC diagnoses were considered to be malignant groups together (15). In our study, the sensitivity, specificity and accuracy rates were 74.7%, 88.16% and 84.76%, respectively. False positivity is generally below 5% in publications, but false negativity ranges varies between 0-16% (16,17). However, when we look at the current publications (Table 5), the false positivity is between 3.5-11.90, while the false negativity is 2.3-42.11 (2,3,7-14). The fact that the publications made in the last 10 years have higher results than previous publications has been linked to the increase in the number of thyroidectomy operations performed (18).

The vast majority of false-negative results is insufficient sampling, and the reason for this is that PTMCs

Table 4. Case numbers and rates of true negative, true positive, false negative and false positive cases

	Cytologic diagnosis	Histologic diagnosis	Cases with cytologic-histologic diagnosis imcompatibility
Benign case grup	237	216 (65.85%) (TN)	21 (6.40%) (FN)
Malign case grup	91	62 (18.90%) (TP)	29 (8.84%) (FP)
Total case number	328	278	50

TN=True negative, FN=False negative, TP=True positive, FP=False positive

Table 5. Comparison of the literature with this study

Literature	Year	Case number	Sensitivity	Specificity	Accuracy	Negative predictive value	Positive predictive value	False positive	False negative
Haberal et al.	2009	260	92.6	91.6	91.9	96.5	83.5	5.7	2.3
Muratlı et al.	2013	126	87.1	64.6	77.3	79.5	76.1	15.5	7.3
Ugurluoglu et al.	2015	1096	93	79	88	85	90	8.19	3.82
Rong et al.	2016	2 043	87.1	95.3	91.0	-	-	4.7	12.9
Wang et al.	2017	629	96.67	89.76	92.75	87.88	97.22	-	-
Roy et al.	2019	112	81.48	95.29	91.16	94.18	84.61	3.5	4,46
Erkinüresin et al.	2020	149	57.89	88.10	82.52	90.24	52.38	11.90	42.11
Pandey et al.	2020	447	57.14	90	80.28	70.58	83.33	11.60	9.8
Guo et al.	2020	5729	98.8	60.5	97.7	59.1	98.9	-	-
Anand et al.	2020	646	72.4	94.3	87.9	89.2	84	4.04	8.08
This study	2020	328	74.7	88.16	84.76	91.14	68.13	8.84	6.40

can't be caught with FNAB. The false negativity rate in this study was 6.40% and was in line with the literature (2,3,7-14). The current study, PTMCs were the most common cause of false negativity in line with the literature (2,3,7-14). The current study, 58.33% of malignancies detected in the FN/SFN group, 84.21% of the MC group, 58.33% of the AUS/FLUS group and 72.72% of the BC group were PTMC cases that were more distant from the investigated nodule. For this reason, there may be publications stating that these lesions should be excluded in the evaluation of FNAB, since it may be misleading in terms of false negative diagnosis (15,16). If PTMCs are not evaluated in this study, sensitivity increases from 74.7% to 92.16%.

Our false positivity rate was 8.84, and as the closest result in the literature is 8.19 and is belonged to Ugurluoglu et al. (8). When we look at the current literature, the highest result is 15.5 and is belonged to Muratlı et al. (7). In the literature, the cytological-histopathological incompatibility rate is quite high when it comes to follicular lesions (1-20). Fine needle aspiration biopsy is particularly sensitive in detecting papillary, medullary, anaplastic carcinoma, poorly differentiated follicular and insular carcinoma, while the sensitivity decreases and the false positivity increases in lesions such as adenomatous nodules, FA, well-differentiated FC, HT and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) which have similar cytological features (7).

The number of false positive cases in this study was 29, and 19 of them consisted of follicular lesions that could not be distinguished cytologically in accordance with the literature. The compatibility rate with histopathology of Han K et al. in the FN/SFN series of 116 cases were only 44%. Incompatible lesions were 40% TPC and 15% NG in this FN / FNK series (21). The compatibility rate in this study was 36% in the FN/SFN series while incompatible lesions were 30% PTC+PTMC and 33% NG in the our FN/SFN group.

Noninvasive encapsulated follicular variant of papillary thyroid carcinoma, another follicular lesion in which nuclear features of papillary thyroid carcinoma (NFPTC) is seen, is named as NIFTP according to the 2017 WHO Classification (19). If NFPTC is multifocal rather than diffuse distribution in this lesion and if the lesion is subcapsular, it will not be reflected in

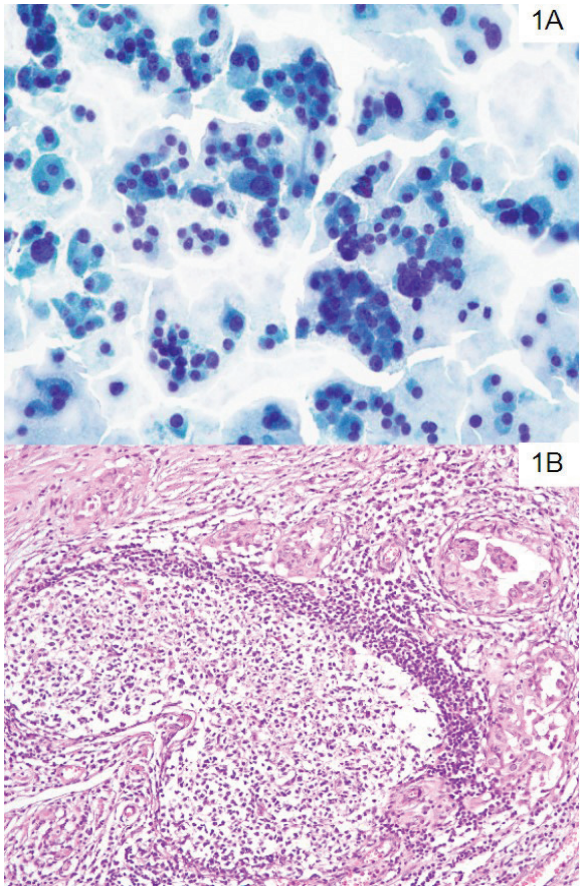

Figure 1. 1A- high cellularity in a lymphocyte-free background, pronounced atypia in the oncocytic character, focal pseudoinclusion. 1B- Focal lymphoid follicles and oncocytic follicular dysplasia in the excision.

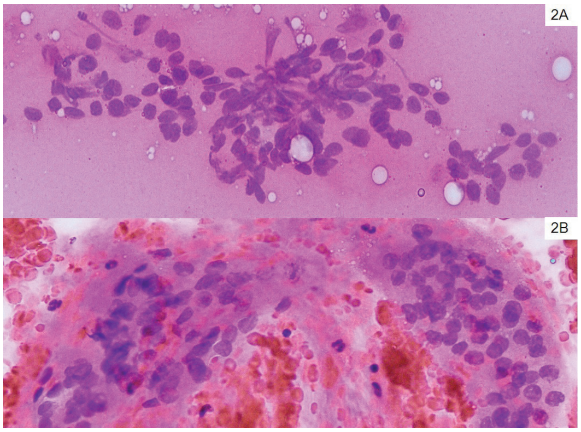

Figure 2. 2A- Air drying artifact in nodular goiter.
2B- Air drying artifact in bleeding areas, chromatin clearing and pseudoinclusion.

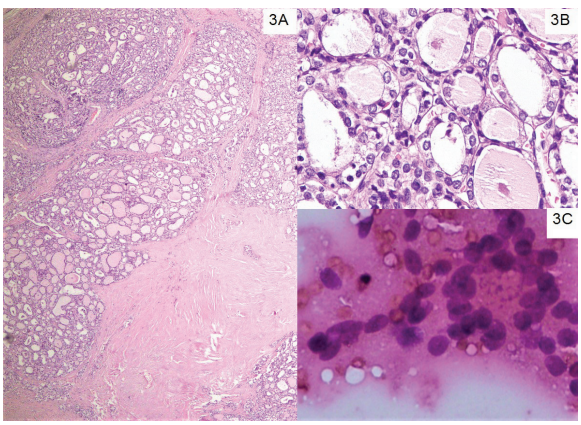

Figure 3. 3A-Intense fibrosis in the aspiration area. 3B,3C-Cells showing nuclear enlargement, chromatin clearing and groove in the rebiopsy area.

the aspiration, so it can be diagnosed as benign hyperplastic nodule, AUS/FLUS or FN/SFN (19). In this study, prominent syncytial pattern and microfollicular appearance were observed in 1 NIFTP diagnosed with FN/SFN in FNAB, and therefore, the suspicion of NIFTP was mentioned in the pathology report interpretation. Aron et al. stated that microfollicular appearance and syncytial pattern were quite specific in the diagnosis of NIFTP (22).

Hashimoto thyroiditis, may be confused with hurthle cell neoplasia, follicular neoplasia, lymphoma and PTC depending on the percentage of oncocytic cells, lymphocytes and ordinary follicular cells it contains (4). In our study, 2 of the HT were diagnosed with SM and 1 with MC, and they mostly caused differential diagnosis problem with papillary carcinoma. High cellularity and prominent atypia in the oncocytic character were observed 1 HT case, who was diagnosed with MS in cytology, but no lymphocytic infiltration was observed in the background. In the excision of this case, PTC was not seen, but in addition to HT, multifocal oncocytic follicular dysplasia foci, which were the precursors of PTC, were observed (Figure 1). It has been reported in the literature that these follicular dysplasia foci may be precursors to PTC (23). It is stated that they also include RET/PTC gene rearrangement molecularly and are also responsible for the development of microscopically detected multicentric PTCs (23). It should also be kept in mind that the oncocytic variant PTC may develop on HT background and the differential diagnosis of these two lesions may be difficult (23).

Another reason for false positivity may be due to the fact that NFPTC can be observed in benign lesions as focal or can be seen as artifactual. In air drying artifact, especially in hemorrhagic lesions, chromatin

clearing and pseudoinclusion are common findings (24) (Figure 2). Repeat biopsies can also create reactive morphological changes in cells such as nuclear enlargement, chromatin clearing and groove (25,26). In our study, similar views were observed in an NG case with a history of rebiopsy (Figure 3).

One of the number of improvements have been introduced with the 2017 thyroid Bethesda System was as follows: The "usual management" of AUS/FLUS and FN/SFN now includes the option of molecular testing (19). The European Thyroid Association has determined molecular panel (including at least BRAF, NRAS, HRAS, KRAS, PAX8/PPARG, RET/PTC) which diagnostic value in the evaluation of thyroid nodules of uncertain cytology (27). In studies performed when BRAF, NRAS, HRAS, KRAS, PAX8/PPARG and RET/PTC were added to cytology in AUS/FLUS, FN/SFN group or indeterminate FNA cytologies, it was observed that sensitivity, specificity, negative and positive predictive values increased from 18 to 100%, from 82 to 100%, from 56 to 100%, and from 19 to 100%, respectively (27). Besides helping to clarify whether or not one is dealing with a malignant tumor, the detection may guide the type of surgery (27).

Since our study was a retrospective study, evaluation was made with the available data and since some cases did not reach the follow-up and their excisions despite the diagnosis of MC in cytology. For this reason, malignancy rates are low in view compared to the literature. Since ultrasound information, lesion size, solid-cystic component and localizations are not evaluated, a clear interpretation can not be made regarding sampling failure.

The experience and training of the doctors applying the FNAB has been shown to be a most important factor adequacy of the FNAB sample. Yusef et al. showed that when a physician and pathologist lacked training, the incidence of insufficient specimens for diagnosis was up to 29.5%, compared to 4.6% when samples were taken by properly trained doctors (28). In addition, the importance of urgent cytological evaluation of aspiration samples made by an interventional radiologist in obtaining sufficient material was shown (29). Urgent cytological evaluation is especially important in FNABs performed using imaging methods such as endoscopic ultrasound guidance (30).

CONCLUSION

Fine needle aspiration biopsy is an easy-to-apply, minimally invasive, cheap and diagnostic tool with high diagnostic accuracy. The reasons for the decrease in FNAB efficiency are insufficient sampling, inexperience of cytopathology, difficulty in distinguishing follicular lesions and benign lesions mimicking PTC. The leading cause of false negative results in the current study are PTMC cases that were not caught by aspiration. The most common cause of false positivity is malignancy imitating lesions and follicular lesions that cause differential diagnosis in FNAB. As the experience of the clinician and cytopathologist increases, the correct diagnosis rate may increase and the number of unnecessary thyroid operations may decrease. At the same time, we think that the confidence in thyroid FNAB's will increase with the participation of molecular methods applied to FNAB's in some centers recently. For cytologically indeterminate nodules, it is important to detect BRAF, RET/PTC, PAX8/PPARG and RAS mutations.

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Conflict of Interest

The authors declare no competing interest.

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