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Original Research Article

Fine needle aspiration cytology comparison of diagnosed thyroid nodules diagnosis with postoperative histopathology

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ABSTRACT

Background: Around 2.5% of male cancer in Turkey, 12% of female cancers include cancers of the thyroid. Early diagnosis and correct treatment of thyroid cancers is therefore important. However, in addition to preventing the complications, patients not to be subjected to unnecessary thyroid procedure depend on the pre-detection of that whether the nodules are benign or malign. The objectives of the study were to investigate whether fine needle aspiration (FNA) cytology of thyroid nodules is sufficient for diagnosis. Thyroid FNA result is based on the standardized Bethesda System for Reporting Thyroid Cytopathology (TBSRTC).
Methods: FNA cytology reports of 1808 patients for the period between January 2011 and December 2017 in Atatürk City Hospital, which is located in Balıkesir province, in the western part of Turkey, were retrospectively analyzed. Cytology results were reported as follows: non-diagnostic, benign, atypia (AUS) or follicular lesion (FLUS) of undetermined significance, follicular neoplasm or suspected follicular neoplasm (FN), suspected malignity and malign. They were compared with postoperative histopathology result.
Results: According to the thyroid FNA cytology, 409 patients were operated on, and the obtained specimens were histopathologically analyzed. The histopathological malignity rates of patients were detected to be as follows: 0.0%, 2.0%, 3.0%, 12.1%, 31.3% and 51.5%. It was detected that malign thyroid cancer was detected to be seen more in women and the age group of 31-60. The sensitivity value of the research was detected to be 92%, which was a significantly high ratio. Positive and negative predictive values were detected to be 97% and 92%, respectively.
Conclusions: Where FNA cytology result is insufficient, FNA procedure should be repeated. FNA must be repeated with USG for cases with suspected AUS, FLUS and follicular neoplasm.

Keywords: Bethesda system for reporting thyroid cytopathology, Fine needle aspiration cytology, Histopathology, Thyroid

INTRODUCTION

In Turkey thyroid cancers rank number nine with a rate of 2.5% within the most frequent types of cancers for male patients, while it is ranked as the second, after breast cancer, with a rate of 12% within the most frequent types of cancer for female patients. According to the data provided by Ministry of Health for 2014, the incidence rate is 20.7 in 100.000 (0.0207%).[1] Thyroid nodule is seen in 5.3-6.4% of male patients, and 0.8-1.6% of female patients.[2-5] It was reported that approximately 1.7-7% of the thyroid nodules were detected to be malign.[4-7] Clinical data is obtained in a satisfactory level with regards to the nodules thanks to physical examination, thyroid function tests, ultrasonography and scintigraphy examinations. However, identification of the nodules as benign or malign can be done with histopathological evaluation with Tru-cut biopsy or fine needle aspiration

biopsy of thyroid. Slow progression of thyroid cancers and patients to live longer with early treatment reveals the significance of early diagnosis. For cytological examination, FNAB is frequently applied for being well-tolerated by patients and easily applicable. A final diagnosis can be established on 70-75% of the nodules as benign or malign, by using FNA cytology.[7-9] For the diagnosis of thyroid nodules, a standardization was ensured by using standard bethesda system for reporting thyroid cytopathology.[9,10] Due to providing reliable results, having lower costs and being an efficient, minimal invasive method, as well as being easily tolerated by the patients, FNAB is the first choice in the diagnosis of thyroid nodules.[11-13]

Additionally, tru-cut biopsy method, with a higher reliability, started to be used for deep and non-palpable nodules in the recent studies. However this method is highly painful, which takes a longer time and requires a Radiologist or Endocrinologist. Furthermore, there are also studies suggesting that there is no difference between the pain level of FNAB and Tru-cut on the 5th and 20th minutes of the procedure.[14,15] In this study, our objective is to approve the reliability and sensitivity of FNA cytology, performed with clinical examination, by comparing it with the post-operative histopathology report.

METHODS

In our study, the cytology reports of 1808 patients, on which FNAB was applied due to thyroid nodules bin Balıkesir Atatürk City Hospital between January 2011 and December 2017 were retrospectively analyzed. All the samples taken after surgery included in these reports were fixed in 10% phosphate buffered formaldehyde and stored in paraffin. Moreover, the sections obtained from the samples were stained with hematoxylin and eosin and then prepared for routine light microscopy. In addition, they were stained with Papanicolaou (PAP), May-Grünwald Giemsa.

Then, all the samples were evaluated and reported by an expert pathologist. Cytology reports of 196 patients were excluded from the evaluation for not having thyrosite, but having the analysis of blood and respective elements. The presence of 5-6 separate group follicle cells consisting of at least 10 cells without artifact was considered as the criterion of adequacy. Cytological evaluation revealed presence of colloid on the ground, cell density, cell size, pleomorphism, cohesion, nucleus/cytoplasm ratio, nucleus characteristics, chromatin properties, cytoplasmic staining characteristics, presence of necrosis and inflammation cells. In the evaluation process where cytology samples were painted with Papanikolaou (PAP), May-Grünwald Giemsa (MGG) and using BSRTC, the results were classified as follows: non-diagnostic, benign, atypia of undetermined significance (AUS) or follicular neoplasm of undetermined significance (FLUS), suspected follicular neoplasm (FN), suspected malignity and malign. Hematoxylin and eosin stained preparations of 409 cases who underwent thyroidectomy after FNAB were reevaluated and the diagnosis was confirmed. FNAB and histopathological results were compared. When comparing FNAB and histopathological results, diagnostic value, specificity, sensitivity, positive predictive value and negative predictive value were calculated.

Statistical analysis

The data obtained from this study were transferred to the SPSS program (Version 25.0; SPSS Inc., Chicago, IL, USA) and then analysed. The number, percentage, mean and standard deviation values were utilized for the evaluation of descriptive statistics.

RESULTS

After examining the cytology samples of 1612 patients, the results were identified to be as follows: non-diagnostic 13.8% (223), benign 74% (1.195), atypia of undetermined significance 3.4% (AUS) (56), follicular neoplasm 3.1% (50), suspected malignity 2.3% (37), malign 3.2% (51) (Table 1). The youngest one of 1334 patients, on whom FNAB was applied, was 16 years old, while the oldest was 86, and the age average was 49.78±13.20. Within 278 patients, the youngest male patient was 19 years, while the oldest was 85, and the age average was 55.44±12.79. It was detected that the malignity related diagnosis was conferred more within the age group of 31-60 (Table 2).

Examining histopathologically the thyroidectomy material of 409 patients undergoing an operation after FNA cytological examination, the malignity rates were detected to be as follows according to their cytological diagnosis groups: non-diagnostic group 0% (0), benign group 2% (2), atypia of undetermined significance 3% (3), follicular neoplasm or lesions suspicious for follicular neoplasm 12.1% (12), suspected malignant 31.3% (31), malign group 51.5% (51) (Table 3).

Around 80 of 99 patients were women, while 19 were male, who were diagnosed to be histopathologically malign. Distribution of these patients by age group is as follows: 7 patients between the age of 0-30, 68 patients between the age of 31-60, 24 patients between the age of 60 and older. The validity, sensitivity, specificity of pre-operative thyroid FNA cytological examination to post-operative diagnosis, including the positive and negative predictive values were analyzed. These values were detected to be as follows, respectively in our study: 98%, 92%, 99%, 97% and 92%.

Table 1: Cytologic diagnosis sex distribution.

Sex	Total	Nondiagnostic	Benign	Atypia of undetermined significance	Follicular neoplasm/ suspicion	Suspicion of malignancy	Malignant
Women	1334	175	1012	42	40	26	39
Men	278	48	183	14	10	11	12
Total	1612	223	1195	56	50	37	51

Table 2: Age distribution of cytological diagnosis.

Age	Total	Nondiagnostic	Benign	Atypia of undetermined significance	Follicular Neoplasm/ Suspicion	Suspicion of malignancy	Malignant
0-30	129	30	82	7	5	2	3
31-60	1078	135	815	33	33	26	36
>60	405	58	298	16	12	9	12
Total	1612	223	1195	56	50	37	51

Table 3: Cytologic-histologic correlation.

Cytological diagnosis	Number of patients operated with	Benign	Papillary carcinoma	Follicular carcinoma	Medullary carcinoma
Nondiagnostic	55	55	0	0	0
Benign	198	196	2	0	0
AUS	28	25	2	0	1
FN	40	28	8	1	3
Suspicion of malignancy	37	6	28	1	2
Malignant	51	0	43	2	6

DISCUSSION

Thyroid nodules are one of the most frequently seen endocrine pathologies. It was stated that the thyroid nodules in in the childhood was seen to be less (0.2-5%) compared to adults. Ultrasonography and autopsy examinations performed on the adults showed that the thyroid gland comprises of 25-40% nodules. However, while the cancer diagnosis rate was stated to be between 5–15% for thyroid nodules of suspected adults, this rate was conferred to be between 22–26% for children compared to adults. The American Thyroid Association (ATA) suggests FNAB accompanied with USG on thyroid nodules with a diameter larger than 10 mm, while suggesting FNAB accompanied with USG for thyroid nodules smaller than 10 mm, provided that suspected USG image is available.[16-19]

For our study, this ratio was detected to be 2%. Thyroid cancer is seen 3 or 5 times more frequent in women, compared to men. In our study, the women with thyroid malignity as compared to men was found to be 80/19=4.21, which is in compliance with the rates declared in the literature.[20,21] For our study, this ratio was detected to be 2%. Thyroid cancer is seen 3 or 5 times more frequent in women, compared to men. In our study, the women with thyroid malignity as compared to men was found to be 80/19=4.21, which is in compliance with the rates declared in the literature.[22,23] Age and gender are critical criteria with regards to nodule malignity. For women under the age of 30, the malign nodule possibility is lower, while the malignity of nodules increases by percentage, which is more typical for men. FNAB is an affordable, easy-to-apply and effective diagnosis method, identifying the thyroid nodules as either benign or malign. In our research, the sensitivity of FNAB was found to be significantly high (92%). FNAB is performed by surgeons, most of which are detected with palpation. FNAB is to be repeated for patients with insufficient or no thyrosite following FNA cytology. For cases with deeply located nodules or not properly palpated, FNAB should be repeated with USG.[23,24] FNAB USG should be repeated for clinically suspected cases, for being well-tolerated by patients. The malignity diagnosis rate is improved in repeated FNABs. Correct guidance for patients ensures such opportunities as early-diagnosis and treatment. FNAB reduces the number of unnecessary operations for benign lesions, while ensuring correct operation time for patients with malign lesions.

Additionally, it prevents the complications of secondary operation. It extends the survival time of patients.[25-27] BSRTC ensures consensus in diagnostic terminology and morphological criteria for pathologists, including suggestions on malignity risks and patient management.[28-31] The rate of malignity incidence is as

follows within the literature: 63-90% of papillary carcinomas, 5-23% of follicular carcinomas, 3-5% of medullary carcinomas, 0.4-10% of hurtle cellular carcinomas, 1-3% of anaplastic carcinomas and 1-2;% of other malignancies.[32-34] In our study, 83 of 99 malign cases (84%) were detected to be as papillary carcinoma, while 4 (4%) of them were follicular carcinoma, 12 (12%) were medullary carcinoma. While the rate of papillary carcinoma incidence was higher, the distribution of rates were in harmony with the ones suggested in other studies; anaplastic carcinoma was not seen in our study, the rate of which is lower compared to other types. In our study, 37 of 37 cases, who were diagnosed to be suspected malign, based on their FNAB results, underwent an operation, and malignity was detected on 31 (84%) of these patients. Due to the malignity risk, bilateral total thyroidectomy (BTT) was performed on cases with suspected malignity.[35,36] 40 of 50 patients, who might have follicular carcinoma within the group of follicular neoplasm or suspected follicular neoplasm, underwent surgery. 12 (24%) of them were detected to have carcinoma. These patients underwent BTT, while those with suspected nodules having total thyroidectomy (UTT), near total thyroidectomy (NTT) for the other side or TT only to the suspected nodule. The rate of post-operative follicular carcinoma incidence is 5-8.9% in the literature, while it was detected to be 4 (4%) in our study.[37] The reason for the patients diagnosed to have follicular carcinoma to be low, while those having medullary carcinoma to be higher is attributed to diet and environmental effects. AUS interpretation rate in a laboratory should be between 3-6% of all thyroid FNABs, according to BSRTC. Reporting AUS in higher rates indicates the over-usage of this category. This rate is 3.5% for our study. 25 of 56 patients, whose cytology were AUS, underwent thyroid lobectomy surgery, while 3 (8%) of them were diagnosed to be malign.[38,39] 198 of patients with benign cytology underwent a surgery, and 2 (1%) of them were diagnosed to have papillary carcinoma. 6 (6%) of the cases, who were detected to have malignity in their post-operative histopathology, underwent the complementary total thyroidectomy surgery. Our study shows that the number of unnecessary thyroid operations is high. We are of opinion that pathologists should suggest re-FNAB for cases with under-diagnosed cytology for preventing patients with benign cytology report to undergo surgeries. The rate of insufficient material is between 10-28% in the literature. For our study, this rate was found to be 13.8%.[40]

For obtaining the correct cytology result for thyroid FNA, there are two critical factors, one of which is the availability of satisfactory samples, while the other one is the availability of experienced cytopathologists. Repeated FNAB for patients with insufficient samples should be performed with USG.[41,42] Given that 2-3% of the patients were detected to have malignity during the follow-up process with insufficient FNAB, it is of vital importance to repeat FNAB on patients with insufficient cytology results.

CONCLUSION

FNAB is a sensitive, reliable, easy-to-apply and affordable, effective diagnosis method, which is used as the first step of diagnosis for examination of thyroid nodules. FNAB should be repeated for cases with insufficient cytology. FNAB must be repeated with USG for cases, whose cytology is detected to be AUS or FLUS. For patients with deeply located nodules, including those whose nodules cannot be detected via palpation, and those with suspected malignity, the FNAB should be performed with USG, thus increasing the sensitivity and specificity. Our study shows that thyroid FNA cytology is a significantly, validity, sensitive and specific method for malignity diagnosis.

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