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ORIGINAL ARTICLE

Correlation of Fine Needle Aspiration Cytology of Thyroid Gland with Histopathological Results

Authors' Contribution:
A–Study Design
B–Data Collection
C–Statistical Analysis
D–Data Interpretation
E–Manuscript Preparation
F–Literature Search
G–Funds Collection

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ABSTRACT:

Fine needle aspiration cytology (FNAC) is considered as the gold-standard diagnostic test in the diagnostics of thyroid nodules. It is a cost-effective procedure that provides specific diagnosis rapidly with minimal complications. It plays an important role in the determination of treatment - patients with suspected malignancy diagnosis can be subjected to surgery. On the other hand, it can decrease the rate of unnecessary surgeries.

Aim: The aim of this study was to evaluate and compare the correlation, accuracy of fine needle aspiration cytology (FNAC) in the diagnostics of thyroid lesions with the final histopathologic diagnosis based on the surgical specimens.

Materials and Methods: In our study we performed a retrospective analysis of a case series of patients who had been admitted to the Department of Endocrine, General and Oncological Surgery of the Hospital of M. Kopernik in Łodź (Poland) between May 2016 and December 2017 and underwent FNAC with subsequent surgery. Cytological diagnosis was classified into six Bethesda categories.

Results: On cytological examination, 1070/1262 cases were reported as benign, 49 as malignant and 143 as suspicious. On histopathological examination, 956/1070 cases were confirmed as benign but there were 114 discordant cases. Among the other cases histopathology diagnosis confirmed malignancy in 45/49 cases and 128/143 suspicious cases. The sensitivity and specificity were 60,28% and 98,05% respectively. False positive rate was 1.95% and false negative rate was 39.72%. The positive predictive value was 90.1% and negative predictive value was 89.35%. Accuracy of FNA in differentiating benign from malignant thyroid lesions was 89.46%.

Conclusions: Fine needle aspiration cytology is a simple, cost-effective and popular procedure for the diagnosis of thyroid cancer. It is recommended as the first-line investigation for the diagnosis of thyroid lesions.

KEYWORDS: fine needle aspiration biopsy, fine needle aspiration cytology, thyroid cancer, papillary thyroid cancer, throidectomy

INTRODUCTION

Fine needle aspiration cytology (FNAC) is the dominant method in the evaluation of thyroid nodules. It is characterized as fast, reliable, minimally invasive, and cost-effective . One of the major advantages is that FNAC can be performed as an out-patient procedure. It is relied upon to distinguish benign from neoplastic or malignant thyroid nodules. According to many analyses it has led to a substantial decrease in the number of surgeries of the patients with thyroid nodules but on the other hand it has contributed to an increase in the percentage of operated malignant lesions [1][2]. Currently, this technique is used in clinical practice worldwide. The limitation of FNAC includes false negative and false positive results. Practitioners should be aware of these potential limitations and pitfalls of FNA interpretation such as specimen inadequacy, sampling techniques and other.

Thyroid cancer is the most common endocrine cancer. The incidence of this disease has dramatically increased worldwide, at higher rate than any other cancer [3].

The purpose of this study was to compare the results of FNAC using the Bethesda System with the final histological diagnosis in order to determine the accuracy of the diagnoses of thyroid neoplastic nodules based on FNAC results.

We evaluated the potential of FNA in differentiating benign and malignant thyroid lesions. Our aim was also to analyse the false positive and false negative diagnosis.

MATERIALS AND METHODS

In our study, the patients admitted to the Department of Endocrine and General Surgery of the Hospital of M. Kopernik in Łodź (Poland) between May 2016 and December 2017, subjected to FNAB first, and then to surgery, were retrospectively investigated.

Only cases of thyroid changes confirmed with FNAC, with subsequent surgery, were included in this study. Patients with other type of swelling than the thyroid neck swelling were excluded. The FNAC results which were inadequate for evaluation were also excluded. Histopathology results were compared with preoperative FNAC report.

Ultrasonography of the thyroid gland, X- ray examination of the chest and thyroid hormone profile were obligatory before surgery. All cases of FNAC and histopathology results were collected. Data were retrieved from the institutional database and analyzed. There were 1262 thyroid FNA results collected during this period. All of the FNAs in the present study were performed under ultrasound guidance. In case of multiple nodules, even if one nodule was malignant and the other was benign, the case was reported as malignant in cytology and classified as malignant.

Cytological diagnosis of the thyroid is influenced by the guidelines "The Bethesda System for Reporting Thyroid Cytopathology" (TBSRTC) [4].

Every report should be classified into one of six diagnostic categories:

- I-nondiagnostic or unsatisfactory
- II- benign
- III- atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS)
- IV- follicular neoplasm or suspicious for a follicular neoplasm
- V- suspicious for malignancy
- VI- malignant

The corresponding histopathology report on the thyroid gland specimen obtained during the operation was available in all cases. A total of 1262 cases who had available both cytology and histopathology reports formed the study group. The statistical analysis included false positive rate, false negative rate, sensitivity, specificity, positive predictive value, negative predictive value and accuracy.

RESULTS

Of 1262 patients constituting the study population, 976 (77.34%) were women, and 286 (22.66%) were men between 18 and 82 years of age (average 50 years old) with female to male ratio of 3.4:1. All patients were subjected to FNAB before surgical treatment. The highest number of cases were seen in the age group of 41-50 years (25.59%) followed by the age group of 51-60 years (22.35%) and 31-40 years (22.19%). The age and sex distribution is shown in Figure 1 and 2.

In cytopathological evaluation according to the Bethesda Classification the results were classified as: I- unsatisfactory, II- benign, III- atypia (or follicular lesions) of undetermined significance (AUS), IV- follicular neoplasm or lesions suspicious for follicular neoplasm (FN),V- suspected malignant and VI- malignant.

Among 1262 specimens of FNAC, 158 (12.52%) were reported as unsatisfactory, 744 (58.95%) as benign, 76 (6.02%) as atypia (or follicular lesions) of undetermined significance (AUS), 92 (7.29%) as follicular neoplasm or lesions suspicious for follicular neoplasm (FN), 143 (11.33%) as suspected malignant and 49 (3.88%) as malignant. This distribution is illustrated in Figure 3.

The specimens of 1262 patients operated after FNAC were histopathologically evaluated, and the malignancy rates in these categories were as follows: for I-st Bethesda group- 9 cases (5.7%), II-nd- 62 (8.33%), III-rd-13 (17.1%), IV-th-30 (32.61%), V-th- 128 (89.51%) and VI-th-45 (91.83%) respectively. The total number of benign lesions was 975 (77.26%) and of malignant lesions 287 (22.74%). The ratio of malignant to benign lesions being 1:3.4.

The correlation between FNAC and final histopathology diagnosis for thyroid lesions is shown in Table I and Table II.

As many as 287 cases out of 1262 were diagnosed as malignant on histopatology. Of these, 196 (15.8%) cases were reported as papillary thyroid cancer , 51 (4.0%) as follicular cancer, 15 (0.9%) as medullary cancer, 8 (0.6%) as anaplastic cancer and 17 (1.3%) as other (Table III). The suspicious cases were included in the malignant category for statistical analysis. Total correlation of all cases is shown in Table IV and Figure 4.

Tab. I. Comparison of FNAC and histopathology of thyroid lesions.

CYTOLOGICAL RESULTS ACCORDING TO THE GROUPS OF BETHESDA CLASSIFICATION		HISTOPATHOLOGY		
		BENIGN	MALIGNANT	DISCORDANT CASES
I	158	149	9	9
II	744	682	62	62
III	76	63	13	13
IV	92	62	30	30
V	143	15	128	15
VI	49	4	45	4
TOTAL	1262	975	287	133

- Statistical analysis was carried out to find out the value of FNAC in detecting malignancy in thyroid swellings.
- Sensitivity = True positive/(True positive + False negative) = 173/(173+114)=60.28%
- Specificity = True negative/(True negative + False positive) = 956/(956+15+4)=98.05%
- Positive predictive value (PPV) =True positive/(True positive + False positive) =173/(173+15+4)=90.10 %
- Negative predictive value (NPV) =True negative/(True negative + False negative) =956/(956+114)=89.35%
- False positive rate = False positive/(False positive + True negative) = 15+4/(15+4+956)=1.95%
- False negative rate = False negative/(False negative + True positive) = 114/(114+173)=39.72%
- Accuracy = True positive + True negative/Total number of cases = 173+956/1262=89.46%

In summary the sensitivity and specificity were 60.28% and 98.05% respectively. False positive rate was 1.95% and false negative rate was 39.72%. The positive predictive value was 90.1% and negative predictive value was 89.35%. The accuracy of FNA in differentiating benign from malignant thyroid lesions was 89.46%.

DISCUSSION

The current study was undertaken to evaluate the correlation between cytology and histopathology. It is important because the treatment is greatly influenced by the FNAC results. Our institution is a surgical referral center. Most of the patients would have had initial workup and referred for surgery of the thyroid gland to our clinic. FNAs are usually obligatory before surgical intervention.

Due to the role of cytological results - they should have a low false-negative rate, acceptable sensitivity and specificity for detection of malignancy with a high negative predictive value [5]. According to literature, the sensitivity of thyroid FNA ranges from 65% to 99% , and the specificity from 72% to 100% [5][6][7]. These results of FNAC can be influenced by the effectiveness of the operator, diagnostic difficulty, classification of suspicious lesions [8][9]. In our study, the cases reported as 'suspicious' on cytology were included in the malignant category for statistical analysis because both lead to surgical management.

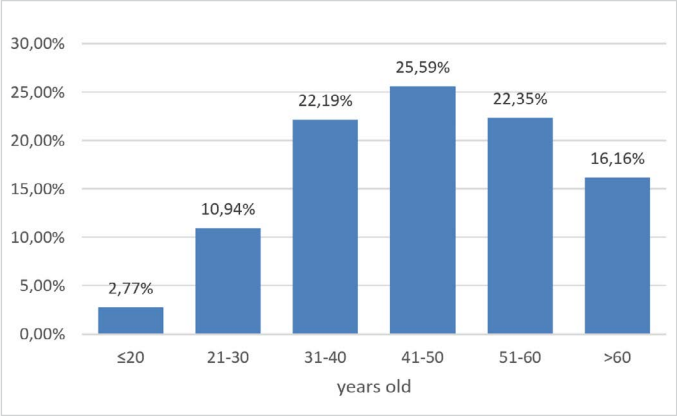

Fig. 1. Age distribution in our study group.

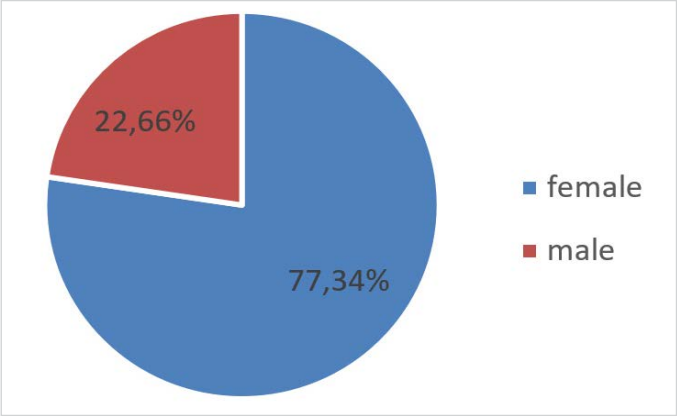

Fig. 2. Sex distribution in our study group.

Tab. II. Details of the discordant cases.

CYTOLOGY ACCORDING TO BETHESDA CLASSIFICATION	NUMBER OF CASES	HISTOPATOLOGIA ZMIANY				
		BENIGN	PAPILLARY CARCINOMA	FOLLICULAR CARCINOMA	MEDULLARY CARCINOMA	OTHER CARCINOMA
I	9 from 158 (5,7%)	-	7	1	-	1
II	62 from 744 (8,3%)	-	44	13	1	4
III	13 from 76 (17,1%)	-	6	3	2	2
IV	30 from 92 (32,6%)	-	12	11	1	6
V	15 from 143 (10,5%)	15	-	-	-	-
VI	4 from 49 (8,2%)	4	-	-	-	-
Total from 1262 cases	133 (10,5%)	19 (1,42%)	69 (5,5%)	28 (2,2%)	4 (0,03%)	13 (1.1%)
% distribution of discordant cases TOTAL 133 cases	100%	14,3%	51,9%	21,0%	3,0%	9.8%

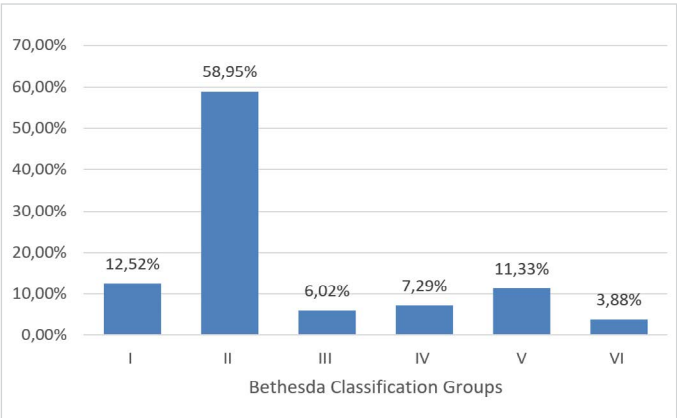

Fig. 3. Distribution of FNA diagnosis.

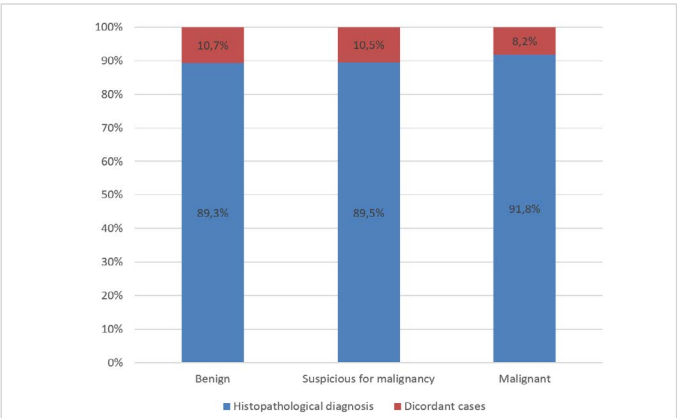

Fig. 4. Cyto-histopathology correlation.

Biopsy is nowadays routinely performed for most cases of thyroid nodules. This is a gold standard in initial diagnosis which has led to a reduction in the number of unnecessary surgeries and consequently to a rise in the percentage of reported malignancies [10]. FNAC can establish a diagnosis based on cytological characteristics. However, it is considered to be "uninterpretable" in 10 to 20% of cases or simply "suspicious" in 9 to 38% of cases [11][12] [13]. That is why diagnosis requires a complete histological examination. According to literature two main drawbacks of the technique are false-negative cytology and failure to detect microcarcinomas either due to an error of interpretation or due to inadequate sampling [14]. Results are dependent also on the operator's experience.

The sex distribution (female/ male ratio of 3.4:1) of the patients in this research is in agreement with the fact that thyroid cancer is more common among women [15][16][5][17][9]. It is a universal phenomenon which can be explained by gender specificity of the disease, the fact that women are usually more frequent visitors to healthcare centers and have medical follow-up for example during pregnancy [18]. But there is also the influence of risk factors such as hormones and lifestyle-negative factors [9][19].

The age range in this study was between 18 and 82 years with the youngest female patient being a case of papillary carcinoma of the thyroid and the oldest patient a female with colloid goitre. Most

Tab. III. Distribution of thyroid cancers.

CYTOLOGY ACCORDING TO BETHESDA CLASSIFICATION	HISTOPATHOLOGY				
	PAPILLARY CARCINOMA	FOLLICULAR CARCINOMA	MEDULLARY CARCINOMA	ANAPLASTIC CARCINOMA	OTHER CARCINOMA
I	7	1	-	-	1
II	44	13	1	-	4
III	6	3	2	-	2
IV	12	11	1	-	6
V	102	16	8	-	2
VI	25	7	3	8	2
Total from 1262 cases	196 (15,8%)	51 (4,0%)	15 (0,9%)	8 (0,6%)	17 (1.3%)
% distribution TOTAL NUMBER OF CANCERS= 287	68,3%	17,8%	5,2%	2,8%	5.9%

of the patients were in the age group of 30-60 years. The highest number of cases were seen in the age group of 41-50 years (25.6%), followed by the age group of 51-60 years (22.3%) and 31-40 years (22.2%). The age distributions of the patients in this research were close to those reported by similar studies [20]. But there is other data which shows that peak age of incidence was in the second, third decades of life or even in the fifth [21].

A delayed diagnosis of thyroid cancer is common because the disease often shows no symptoms in early stages. To diagnose thyroid cancer, the result of a biopsy is required (which is usually performed in case when thyroid cancer is suspected). Unfortunately, screening tests are still limited. Often, the process of diagnosis starts with detection of lumps or sweelings in the neck. It is also likely that increased use of imaging examinations - ultrasonography - has led to the identification of an increasing number of thyroid diseases, especially in younger patients.

In this study 15.2% (143 cases suspected for malignancy and 49 malignant cases) of the cases were suspected in FNAC to be malignant. This observation did not correspond with the studies conducted before, by Her-Junig Wu H et al. (2011) where they reported 5.3 % of 1328 thyroid aspirates to be malignant [22]. Also, the results of other studies are different but in those cases the sample size is different [23][21]. Similar distribution was found in a publication by Chetna S. et al. (2015) where they reported 12.3% of 724 cases to be malignant [5].

The ratio of malignant to benign lesions was 1:3,4, which may have resulted from the fact that we included only cases where FNAC was followed (due to indications) by a surgical resection. Most of the benign cases on FNAC do not undergo subsequent surgical resection if there are no such indications.

In this study, among 1070 FNAC (84.9% from all cases) benign results, colloid goitre was the most common lesion. Among the malignant lesions, papillary carcinoma was the most common 146 (76.0%) followed by follicular carcinoma 31 (16.1%). The increase in the incidence of thyroid cancer is largely due to a rising incidence in papillary thyroid cancer. It constituted around 75% to 85 % of all thyroid cancers, more often in young females [24].

Out of 1070 benign cases in cytological results, 114 (10.6%) were diagnosed to be malignant on histopathology. Out of 49 malignant cases on cytology, 4 (8.2%) cases proved to be benign on subsequent histopathology, and out of 143 cases suspicious for malignancy, 128 (89.5%) were malignant on histopathology. In the study, most of the false negative cases were papillary carcinoma of the thyroid with cystic change that were misdiagnosed and micropapillary carcinoma in the setting of adenomatous goitre.

Benign thyroid changes constitute 77.3 % of all cases in histopathology results (975 cases). The most common thyroid cancer according to histopathology is papillary cancer - 196 cases (68.3% of all diagnosed cancers) followed by follicular cancer - 51 cases (17.7%), medullary cancer - 15 cases (5.2%), anaplastic cancer - 8 cases (2.5%) and other - 17 cases (5.9%).

Among 1262 cases of thyroid swellings that underwent surgery and subsequent histopathological study, 1129 cases showed positive correlation between FNAC and histopathology result. However, it differed in 133 cases when the diagnosis by FNAC proved otherwise. The diagnostic accuracy of FNAC for thyroid swellings in this series was 89.46%.

Benign thyroid changes were the most common in histopathology results (975 cases - 77.3%) (Table II).

The reported sensitivity of thyroid FNA was 60.28 % and the specificity was 98.05%. This indicates that the ability of FNA to detect malignancy in our series was moderate, satisfactory. In addition, there are some studies in the literature reporting sensitivity as low as 55.3% [25]. A similar result was obtained by Musani MA et al., i.e. 61.53% in a group of 105 patients [26]. The reasons for lower sensitivity according to literature can be a combination of the following: operator variability, low number of cases, classification of suspicious lesions and diagnostic difficulty of using FNAC in certain thyroid pathologies [25]. Comparable studies in literature report specificity in the range of 74.9–96% [5].

The positive predictive value in our series was 90.1% compared to 85.7–98.6% in other studies [5,9,27,28] . The negative predictive value in our series was 89.35%, while in similar studies in literature 91.8–94% [5,9,28]. The accuracy of FNA in detecting malignancy in thyroid lesions in our study was 89.46%. Other studies in the literature report accuracy ranging from 83.6% to 93.6% and support our results [5,9,28,29].

Objectively, FNAC can be used as a reliable tool to detect thyroid malignancy.

Tab. IV. Cyto-histopathology correlation of all cases.

CYTOLOGICAL DIAGNOSIS		HISTOPATHOLOGICAL DIAGNOSIS	DICORDANT CASES
Benign	1070	956 TN + 15 cases from suspicious for malignancy	114 FN
Suspicious for malignancy	143	-	15 FP
Malignant	49	128* + 45 = 173 PD	4 FP

TN – True Negative; FN – False Negative; TP – True Positive; FP – False Positive.
*cases suspicious for malignancy

According to authors it is difficult to know the true rate of false-negative results because only approximately 10% of patients with benign cytologic findings are then subjected to surgery [5,6]. In our study, the false negative rate was 39.72% and is higher in comparison to other studies. This can be due to the limited ability of FNAC to accurately diagnose follicular pattern lesions, cystic papillary thyroid carcinoma (PTC) and papillary microcarcinoma [5]. The false positive rate reported in the literature ranges from 6% to 8% [10,27,28]. In our study the false positive rate is very low (1.95%) and comparable with another study, by Chetna Sharma (1.9%) [5]. The reason for this can be the presence of diagnostic features of papillary cancer even in benign conditions like adenomatous goiter, thyroiditis, nodular goiter, follicular neoplasm [5,30]. We observed overdiagnosis of thyroid cancer in 19 cases (for V and VI Bethesda group). Unfortunately, it is evident that more and more surgeries are performed in response to overdiagnosis. Such people are at risk of postoperative complications: even permanent hypoparathyroidism, vocal cord paralysis and other intraoperative complications. Moreover, those patients will also need lifelong supplementation of thyroid hormones and surgical, endocrinological monitoring. The increase in the rate of overdiagnosis of thyroid cancer is already a serious public health concern.

CONCLUSIONS

FNAC is reported to be a safe, simple, rapid and cost-effective method. It can be widely performed without anesthesia in outpatient medical institutions. But it requires proper pathological interpretation. In this study, the effectiveness of FNAC was evaluated through the identification of the correlation between the cytologic diagnoses of thyroid FNAC and the postoperative histopathologic diagnoses.

FNAC is an accurate tool to differentiate a malignant lesion from a benign one with an accuracy of 89.46%. The main problem is the distinction between benign lesions - follicular adenoma, goitre and follicular carcinoma or follicular variant of papillary carcinoma. Another problem is papillary microcarcinoma - usually not detectable at clinical examination and diagnosed incidentally during pathologic examination of thyroid specimens after surgery for benign thyroid diseases. Owing to their small size microcarcinomas can remain undetected in FNA. Nevertheless, as FNAC is considered a screening procedure, particular attention should be paid to the problem of decreasing the number of false-negative diagnoses.

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