

Comparison of Postoperative Histopathological Evaluation and FNAB Results in the Diagnosis of Nodular Thyroid Diseases

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Abstract

Aim: To compare postoperative histopathological evaluation and surgical results of USG guided fine needle aspiration (FNA) in thyroid gland.

Study Design: Retrospective Analysis

Material and Method: 37 patients (10 males and 27 female) aged between 19 and 67 years (mean: 41.91 ± 12.54) who underwent diagnostic thyroid FNA procedure followed by surgical intervention were included in the study.

Results: In 35 patients, palpable nodules of various sizes were detected during clinical examination. In 2 patients, thyroid gland examination was normal. In one of these patients, there was a palpable painless mass underneath the left sternocleidomastoid muscle. The first FNA results, the second FNA results and the post-operative pathology results of the 37 patients included in the study were discussed.

Conclusion: We concluded that FNA under USG guidance is a reliable diagnostic method that should be considered while evaluating thyroid nodules.

Keywords: fine needle aspiration; goiter; thyroid nodul

INTRODUCTION

Fine needle aspiration (FNA) is the best diagnostic method in thyroid nodules. Safety, cost-effectiveness, minimal invasiveness and high sensitivity are among its advantages and it is highly diagnostic. Although there is a general decrease in the number of patients operated since the method became available in clinical practice, the percentage of cases with cancer has increased [1]. The use of aspiration biopsy with 18 gauge needle in the diagnosis of thyroid nodules was introduced in 1930s by Martin and Ellis, followed by the development of needle biopsies where tissue is obtained with Silverman or through-cut needles. However, this approach has not been widely accepted due to the high morbidity, false negative results and the seeding of malignant cells into the needle.

Scandinavian researchers have first identified the current FNA procedure in 1960 [2]. Turkey is in the region of endemic goiter. The abundance of goitrogens and insufficient iodine intake increases the prevalence of both thyroid cancer and other thyroid diseases [3]. The possible increase in thyroid cancer cases following the Chernobyl disaster will be determined in time. Due to the fact that 90% of thyroid cancers are well-differentiated and therefore have a slow progression and good prognosis, and because diagnostic methods are still developing, decreasing the death rates due to this disease will not be difficult [1].

The two most important factors determining the clinical effectiveness of FNA are the experience of the person performing the aspiration and the

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cytopathologist. Insufficient cell aspiration can cause difficulty in diagnosis. For this reason, ultrasonographic guidance is frequently used [1]. In this study the USG guided FNA results were compared to the postoperative histopathological evaluation results and surgical results were discussed.

MATERIAL AND METHOD

37 patients (10 males and 27 female) who underwent diagnostic thyroid FNA biopsy procedure followed by surgical intervention were evaluated within two years sectional period in Vakif Gureba Research Hospital. These patients were evaluated retrospectively with regard to the sensitivity of the FNA and the surgical intervention. During clinical examination, the presence of a palpable thyroid nodule, the characteristics of the nodule (consistency, size, mobility), and presence of cervical lymphadenopathy were evaluated. All patients underwent FNA under USG guidance and thyroid function tests were performed during pre-operative evaluation. The surgery performed and its complications, FNA results before surgery, the need for a second biopsy and the reason behind it and the post-operative pathology results were recorded for all patients. FNA was performed with a 22-23 gauge 10 ml. syringe. The skin and subcutaneous tissue were traversed through one point and the mass was reached, 3-4 ml. of air was taken into the syringe and it was moved forwards, backwards, towards the interior, exterior and oblique directions 4-5 times without letting the needle exit the mass.

Negative pressure was removed slowly after material was observed at the tip of the needle. The syringe was separated before removal of the needle. The aspirate obtained was sprayed onto microscope slides. Slides were fixated with 95% alcohol. The FNA results were compared with the post-operative histopathology results. In our study, we statistically compared the malignancy rates after FNA with the post-operative pathology results. Fischer's exact test was used for statistics and p value <0.05 was accepted as statistically significant.

RESULTS

37 patients consisting 10 males and 27 females aged between 19 and 67 years (mean: 41.91, SD: ±12.54) were included in the study. In 35 patients, palpable nodules of various sizes were detected during clinical examination. There was a single nodule in 15 patients

and multiple nodules in 20 patients. In 2 patients, thyroid gland examination was normal. In one of these patients, there was a palpable painless mass underneath the left sternocleidomastoid muscle. Pre-operative USG evaluation revealed bilateral cystic nodular hyperplasia in 7 patients (18.9%), bilateral multinodular goiter in 13 (35.1%), one solitary nodule in 5 (13.5%), 1 cystic nodule in 3 (8.1%), bilateral nodular hyperplasia in 7 (18.9%), calcified multiple nodules in 1 and 1 solid nodule with widespread lymphadenopathies in the left neck in 1 patient. When the USG-guided FNA results of the patients were evaluated, benign cystic nodular hyperplasia was found in 6 patients (16.2%), benign follicular hyperplasia in 19 (51.3%), benign hyperplastic nodule in 2 (5.4%), benign colloidal hyperplastic nodule in 4 (10.8%), papillary carcinoma in 3 (8.1%), benign solid nodule in 1, suspicious hyperplasia with irregular atypical follicular cells in 1, and benign cystic follicular hyperplasia in 1. A second FNA was needed in 3 (8.1%) patients. In the first of these 3 patients, the first FNA result revealed a suspicious lesion with irregular thyrocytes, and the second FNA result was evaluated as benign follicular hyperplasia. However, the post-operative pathology result was Hashimoto thyroiditis. In the second patient, both FNAs revealed benign hyperplastic nodule, whereas the post-operative pathology result was toxic nodular goiter. In the third patient, the first FNA result was benign follicular hyperplasia, the second was papillary carcinoma, and the post-operative result was papillary carcinoma. The post-operative pathology results of the patients revealed papillary carcinoma in 5 (13.5%), toxic nodular goiter in 4 (10.8%), diffuse microfollicular adenomatous hyperplasia and cystic nodular colloidal stroma in 5 (13.5%), diffuse adenomatous hyperplasia alone in 2 (5.4%), diffuse adenomatous hyperplasia together with ectopic thymus in 1, Hashimoto thyroiditis in 1, follicular adenoma in 1, nodular colloidal hyperplasia in 8 (21.6%), lymphocytic thyroiditis in 2 (5.4%), microcalcified cystic nodular colloidal stroma in 3 (8.1%), microfollicular adenomatous nodule in 1, cystic colloidal nodular stroma together with lymphocytic thyroiditis in 1, cystic macrofollicular colloidal stroma in 2 (5.4%), and nodular adenomatous hyperplasia in 1 patient. When the results of FNA of 3 malignancies out of 37 patients and the postoperative pathologic result of 5 malignancies out of 37 patients were

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compared ($p=0.355$), no statistical difference was found between groups ($p>0.05$). This result confirms that even though the case number is small, FNA is a reliable diagnostic tool. The surgical procedures performed were as follows: right isthmolobectomy in 17 patients (45.9%), left isthmolobectomy in 12 (32.4%), isthmusectomy alone in 1, partial lobectomy in 1, subtotal thyroidectomy in 1, total thyroidectomy in 5 (13.5%) and additional left functional neck dissection in 3 of these previous patients. When post-operative complications were analyzed, reoperation was performed to one patient due to hemorrhage at postoperative 6 hours, and in a diabetic patient who had a left isthmolobectomy, there was hoarseness due to temporary vocal cord paralysis for 3 months.

An elderly patient who had total thyroidectomy and left functional neck dissection due to papillary cancer died on post-operative day 33. When all patients were analyzed for false negative, false positive and suspicious FNA results; false negative result was found in 1 out of 5 patients with papillary carcinoma (20%), there was no false positive result in any patient. The FNA result evaluated as suspicious was found in one patient in whom the first FNA result was "irregular atypical thyrocytes" and the second FNA result came as benign follicular hyperplasia; the post-operative pathology result was Hashimoto thyroiditis. The first FNA results, the second FNA results and the post-operative pathology results of the 37 patients included in the study are shown in Table 1.

Table 1. First FNA procedure, second FNA procedure, and post-operative pathology results and the surgical intervention performed for the patients included in the study (F: Female, M: Male, HP: Hyperplasia, IL: Isthmolobectomy, L: Lobectomy, T: Thyroidectomy, FND: Functional neck dissection)

Patients	Gender/Age	First FNAB Results	Second FNAB Results	Postoperative Pathology Results	Surgery
1	Female/35	BCNH	—	Cystic colloidal nodular stroma together with lymphocytic thyroiditis	Right IL
2	Female/63	BCNH	—	Microfollicular adenomatous hyperplasia and cystic nodular colloidal stroma	Right IL
3	Female/51	Suspicious hyperplasia with irregular atypical follicular cells	BFH	Hashimoto thyroiditis	Right IL
4	Female/39	BFH	—	Diffuse adenomatous hyperplasia together with ectopic thymus	Left IL
5	Female/22	BHN	BHN	Toxic nodular goiter	Left IL
6	Female/27	BFH	—	Cystic macrofollicular colloidal stroma	Partial L
7	Male/32	PC	—	PC(Capsular-pericapsular invasion)	Total T, Left FND
8	Male/25	Benign cystic follicular hyperplasia	—	Nodular goiter	Left IL
9	Male/56	BHN	—	Toxic nodular goiter	Right IL
10	Female/35	BCHN	—	Lymphocytic thyroiditis	Left IL
11	Male/29	BFH	—	Microfollicular adenomatous hyperplasia and cystic nodular colloidal stroma	Left IL
12	Female/42	BFH	—	Microfollicular adenomatous hyperplasia and cystic nodular colloidal stroma	Left IL
13	Female/67	BFH	—	Nodular adenomatous hyperplasia	Total T

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14	Female/41	BFH	—	Toxic nodular goiter	Left IL
15	Female/48	BFH	—	Microcalcified cystic nodular colloidal stroma	Left IL
16	Female/39	BFH	—		Left IL
17	Male/30	BCHN	—	Microcalcified cystic nodular colloidal stroma	Left IL
18	Male/54	BSN	—	Follicular adenoma	Right IL
19	Female/33	BCHN	—	Nodular hyperplasia	Left IL
20	Female/41	BFH	—	Toxic hemorrhagic cystic nodular goiter	Total T
21	Male/39	BFH	—	Macrofollicular nodular colloidal thyroiditis	Right IL
22	Female/57	BFH	—	Nodular colloidal hyperplasia	Subtotal T
23	Female/42	Benign colloidal hyperplastic nodule	—	Diffuse adenomatous hyperplasia with cystic nodular degeneration	Right IL
24	Male/49	BFH	—	Diffuse adenomatous hyperplasia with cystic nodular degeneration	Left IL
25	Female/40	BFH	—	Diffuse and adenomatous hyperplasia	Right IL
26	Male/62	BFH	PC	PC	Total T, Left FND
27	Male/67	PC	—	PC	Total T, Left FND
28	Female/25	Benign colloidal hyperplastic nodule	—	Microfollicular adenomatous nodule	Isthmo-dectomy
29	Female/57	BFH	—	Nodular hyperplasia	Right IL
30	Female/37	BFH	—	Nodular hyperplasia	Right IL
31	Female/19	Benign colloidal hyperplastic nodule	—	Nodular colloidal stroma	Right IL
32	Female/56	BFH	—	Microcalcified cystic nodular colloidal stroma	Right IL
33	Female/32	BCHN	—	Lymphocytic thyroiditis	Right IL
34	Female/44	BFH	—		Right IL
35	Female/39	Benign colloidal hyperplastic nodule	—	Diffuse adenomatous hyperplasia	Right IL
36	Female/37	BFH	—	PC	Right IL
37	Female/42	PC	—	PC	Right IL

DISCUSSION

FNA performed under USG guidance is an alternative method for conventional FNA, and is a biopsy method with a higher diagnostic value in the evaluation of non-palpable nodules and in nodules with non-diagnostic results from conventional FNA. Non-diagnostic and false negative diagnoses obtained with conventional FNA mostly consist of cystic nodules. This situation once more demonstrates the diagnostic value of FNA

under USG guidance in the evaluation of complex (solid-cystic) thyroid nodules. Apart from being a highly effective diagnostic method in non-palpable or hardly palpable nodules, the value of FNA under USG guidance has increased in the recent last years, particularly in the diagnosis of complex thyroid nodules. Braga et al [1] have investigated the effectiveness of FNA under USG guidance in a study comprising 113 patients with 124 nodules. They reported that the procedure provided

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sufficient aspirate for cytological evaluation in 94% of the nodules and have reached the conclusion that this method is highly effective. The authors have stated that FNA under USG guidance is an excellent diagnostic method for the evaluation of complex nodules. In FNAs performed without USG guidance where results are non-diagnostic, the repetition of FNA increases the chance of diagnosis by 50% each time. Here, the benefit of FNA under USG guidance is indisputable. However, we encounter a diagnosis of insufficient material at a 4-16% rate in cellular preparations [2]. Alexander et al., in a study lasting 6 years, have found a non-diagnostic rate of 13% for FNA under USG guidance and have stated that the highest probability of non-diagnosis is seen in nodules with high cystic content. In nodules with a cystic component of 75% and above, the non-diagnostic FNA rate can rise up to 36% [2].

Other factors affecting the success of FNA include small nodule size; the position of the nodule in the thyroid gland, patient's age and the condition of the neck region. A second FNA under USG guidance, following a non-diagnostic one, achieves a diagnostic sampling in 63%. The high non-diagnostic FNA rates in cystic thyroid nodules are due to the scant amount, or absence of, follicular cells. For many years, simple aspiration of the fluid was thought to be an effective method in the diagnosis and treatment of cystic nodules. Today, the use of high resolution USG has enabled us to understand better the nature of the cysts and realize that many lesions initially evaluated as cystic masses can actually be more complicated structures. In our study, we found cystic lesions in 10 patients out of 37 (27%). Seven of these were bilateral cystic nodular hyperplasia (70%) and 3 were single cystic nodules (30%). The fact that the complex cases comprised 70% of the cases implies the importance of FNA under USG guidance. The results labelled as "non-diagnostic" or "insufficient" are usually encountered as follicular neoplasms or suspicious hypercellular smears. One of the advantages of FNA is that it can easily be repeated within 3-4 months if the first biopsy result is insufficient. If the biopsy result is clearly benign, the patient should be followed-up with suppression treatment. The use of FNA has resulted in an increase of thyroid cancer incidence in the surgical pathologic results from 14% to 29%, and has lowered the treatment and care costs by 25%.

Evaluation of literature shows approximately a rate of 20% for non-diagnostic or insufficient results [2]. In a study by Alexander et al. [2] including a total of 1128 patients with 1458 nodules, 950 of the patients were diagnosed with 1269 aspiration procedures, but the authors were unable diagnose 178 patients with 189 aspirations. They have explained this situation by referring to the presence of cystic component and its density. Non-diagnostic material results are encountered in spite of FNA procedures performed under USG guidance, especially in nodules with a high cystic component. However, this has been minimized by successful and repetitive aspirations [2]. The fact that no result was non-diagnostic despite the presence of cystic components in 10 patients out of 37 (27%) patients in our study can be due to the low number of cases. Thyroid nodules are seen in more than half of the adult population and prevalence increases with age. Although nodular thyroid disease is frequent in the general population, the chances of these nodules being malignant is not high. In some autopsy studies, the thyroid nodularity was found to be 37% and 12% of these were detected to be a single nodule. The chances of encountering thyroid nodular disease clinically are 4-5% in the general population. Only 3.5% of these are malignant. In spite of the low malignancy rate, differential diagnosis of the nodules should always be performed. After establishing the clinical characteristics, the consistency, fixation, the state of the cords, the presence of compression findings and the state of the neck region lymphatics, a FNA should be performed [3]. In assessing the patients with a thyroid nodule of 1 cm and above, TSH serum level should also be evaluated together with FNA under USG guidance. This approach facilitates the diagnosis of thyroid cancer. In studies, the rate of malignancy in cases with non-diagnostic results is reported to range between 5-10%. Alexander et al. [2] report this rate as 5%, and all of the cases were detected as papillary carcinoma. The authors have established a low malignancy rate in nodules that show a decrease in diameter or maintain the same size over time.

Sclabas et al. [4] reported that the false negative, false positive and non-diagnostic rates in 240 patients. They reported a low false positive rate of 4% in this large series. In literature this rate is reported as 0-9%

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[4-10]. Sclabas et al. friends have found hyalinized trabecular adenoma morphology in 2 patients out of the 3 false positive cases, and have confused them with papillary carcinoma. The other third case was a controversial one; there was no vascular and capsular invasion and cytological characteristics were in favor of papillary carcinoma, and this caused a misdiagnosis of the lesion which was post-operatively diagnosed as metastatic follicular carcinoma. The false positive rates in our study were parallel to the ones in literature. In the same study, false negativity was found in two patients (4%). This is in accordance with the rates of 2-7% in literature [4-10]. In our study, this rate was established as 20%, which can be explained with the low number of cases.

The results of FNA procedures indicated 3 malignancies out of 37 patients, whereas the results of the pathological examination detected 5 malignancies out of 37 ($p=0.355$) and we found no statistical difference between the two groups ($p>0.05$). This result shows that, in spite of the small number of cases, FNA was diagnostically reliable in our series.

Scalabas et al., while interpreting the non-diagnostic FNA cases, have realized that the presence of sclerosis, calcification, wide degenerative areas and necrotic structure in the nodule rendered aspiration difficult [4] and concluded that if aspiration is performed by skilled hands under USG guidance and is evaluated by an experienced cytopathologist, the false negative or positive rates would be very low. The treatment of patients with follicular and Hurthle cell neoplasm who do not have autonomic symptoms is still controversial. In thyroid nodules 2 cm and below, in patients younger than 45 years of age, observing with follow-up or partial thyroidectomy can be preferred. The patients to be observed should be followed with high resonance USG. If surgery is preferred, intraoperative frozen sections should be performed; if there are no histological signs of invasive carcinoma and preoperative USG results are normal, it should be kept in mind that the opposite lobe can be left intact during operation. If invasive carcinoma is detected during histopathological examination, the decision of re-operation should be made according to the patient, the tumor factors and risk factors. On the other hand, if the patient is 45 years of age or older and the FNA results display follicular Ca or Hurthle cell neoplasms or if the diameter of the nodule is greater than 2 cm, the

risks and benefits of total thyroidectomy versus partial thyroidectomy should be discussed. If the patient does not have concerns about being hormonally dependent and is above 45 years of age and the nodule diameter is greater than 2 cm, then total thyroidectomy should be preferred [11,12].

CONCLUSION

Although FNA has some unfavorable aspects such as being non-diagnostic at times (which may necessitate the repetition of the procedure), the probability of false results (although the rate is very low) and the need of experienced personnel and cytopathologists, it is a diagnostic method that should be performed for pre-operative diagnosis and for deciding the kind of surgery to be performed. In our study; the results of FNA procedures indicated 3 malignancies out of 37 patients, whereas the results of the pathological examination detected 5 malignancies out of 37 ($p=0.355$) and we found no statistical difference between the two groups ($p>0.05$). This result shows that, in spite of the small number of cases in our study, FNA was diagnostically reliable in our series. The rate of false negatives in our study was 20% and we attributed this to the small number of cases; on the other hand, the false positivity rate was similar to literature.

Based on the findings in our study, we concluded that FNA under USG guidance is a reliable diagnostic method that should be considered while evaluating thyroid nodules.

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