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Original Article

Comparison of cytology reports of FNA cases in thyroid nodules presented separately by two pathologists with the results of thyroid surgery

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Abstract

Introduction: Thyroid nodules are one of the most common clinical conditions. Needle aspiration is used to detect malignancy. This study aimed to determine the diagnostic accuracy of fine needle aspiration in thyroid nodules.

Methods: In this cross-sectional study, fine needle aspiration slides of 115 patients were examined by two independent pathologists and the results were reported according to the Bethesda System. Then, the diagnostic accuracy of the cytological results of fine needle aspiration was compared with the pathology result of the surgical specimen.

Results: A total of 115 patients were assessed, with a mean age of 40.12 years. Most cases were female (84.35%), most were unilateral and on the right side (50.4%) and the mean TSH was 2.13±1.1 in the study patients. The first pathologist reported 39.13% and 60.87% of cases, respectively benign and malignant while the second pathologist respectively reported 52.63% and 63.48% benign and malignant. Kappa agreement coefficient between the two pathologists was 0.69 for the diagnosis of benign and malignant cases in thyroid nodules. The diagnostic accuracy of the first and second pathologists was 79.13% and 90.43%, respectively, in comparison with surgical pathology samples.

Conclusion: The pathologist has a crucial role in differentiating benign and malignant nodules in FNA specimens and preventing surgery.

Introduction

Thyroid nodules are common clinical finding with a prevalence rate of 4%-7% based on physical examination (1), while up to 70% can be identified using ultrasound (2).

These nodules are usually benign (3), but 8%-16% of them are malignant. The risk of malignancy is higher in individuals without clinical symptoms, increasing the clinical significance of research on these nodules (4).

In the past three decades, the prevalence of malignant thyroid nodules and thyroid cancers has increased 2.4-fold (5-6), probably due to improved physical examination and the better quality of ultrasound (7-8).

The method of choice for the evaluation of thyroid nodules is fine-needle aspiration (FNA). Various studies introduce FNA as the first diagnostic procedure which reduces the need for radioisotope scan and thyroidectomy and, thus, reducing costs (9-10). However, some studies showed that, as a preoperative diagnostic procedure, thyroid FNA lacks the sufficient sensitivity for diagnosing malignancies (11).

Recent years have witnessed a rise in applying FNA in Iran. To determine the diagnostic value of FNA results, especially in cases where the patient is referred for surgery, a precise evaluation is required of the diagnostic accuracy, sensitivity, and specificity, and rate of false positive and negative results of FNA. In the present study, the diagnostic value of FNA in differentiating benign and malignant nodules was compared with pathology results as the gold standard.

Materials and Methods

This research was a cross-sectional study. First, a complete history of thyroid disorders, receiving radioactive iodine, surgery, hoarseness, respiratory symptoms, dysphagia, rapid tumor growth, symptoms of hyper- and hypothyroidism, and benign and malignant diseases in the family was taken from all the patients with thyroid nodules visiting Shahid Beheshti Hospital, Hamadan University of Medical Sciences, Iran, in 2015. Furthermore, a physical examination was performed concentrating on the location, number, hardness and size of nodules; attachment to adjacent organs, and cervical lymph node enlargement. Serum TSH level was measured to differentiate hypothyroidism, hyperthyroidism, and euthyroidism. FNA was performed on patients with solitary nodules, while patients with

multiple nodules underwent ultrasound and suspicious nodules (hypoechocity, irregularity and calcification, or central hypervascularity) were examined using FNA. After physical examination and swabbing the site with ethanol, a certain endocrinologist performed FNA on all patients and biopsy was performed using a 23-gauge needle. A number of aspirations were performed on each nodule in different directions. Then, the specimens were fixed on 8-12 slides, stained using the Papanicolaou and Giemsa method in the Pathology Center, and examined by two experienced pathologists (both with a minimum of 10-year experience as faculty members) in two separate teaching and treatment centers. The cytologic evaluation of FNA specimens was single blind. The specimens were sent to the first pathologist and cytology reports were recorded in the checklist. Then, the specimens were sent to the second pathologists and cytology reports were separately recorded in the checklist. Neither pathologist knew the cytology results reported by the other pathologist (i.e. single blind). Results were then classified according to the Bethesda System (12). All Class 5-6, Class 3-4, and large nodules - solitary or multiple - which were clinically suspicious but reported as benign on the FNA result, in addition to nodules which had pressed adjacent organs, were referred for surgery by the physician.

Pathology report based on surgical specimen was the gold standard for diagnosis based on which the sensitivity and specificity of FNA specimens were calculated. Patients were excluded if they did not show up for surgery or other steps of diagnosis.

Results

Overall, there were 115 patients with the mean age of 40.12 ± 14.34 years (range: 16-82 years), comprising 18 men (15.65%) and 97 women (84.35%). Moreover, 53 patients (46.1%) had nodules on the right side of the thyroid gland, 43 (37.4%) on the left side, 18 (15.7%) on both sides, and 1 (0.9%) on the isthmus. Mean TSH in patients ranged from 0.4 to 5.04 mg/dL (SD=1.1)

Based on FNA specimens, the number of benign and malignant cases were respectively 45 (39.13%) and 70 (60.87%) as diagnosed by the first pathologist, and 42 (36.52%) and 73 (63.48%) as diagnosed by the second pathologist (Table 1). Kappa agreement coefficient between the two pathologists was 0.69 for the diagnosis of benign and malignant cases in thyroid nodules through FNA.

Based on the tests on surgical pathology specimens, 47 cases (40.87%) were benign and 68 cases (59.13%) were malignant.

Results reported by the first pathologist as compared with report of surgical specimens had a sensitivity of 83.82%, specificity of 72.34%, positive predictive value of 81.43%, negative predictive value of 75.55%, and diagnostic accuracy of 79.13%.

Results reported by the second pathologist based on surgical specimens had a sensitivity of 95.56%, specificity of 82.98%, positive predictive value of 89.04%, negative predictive value of 92.86%, and diagnostic accuracy of 90.43%.

From among 68 malignant thyroid nodules, 54 (79.41%) were papillary carcinoma, 7 (10.29%) papillary microcarcinoma, 5 (7.36%) follicular carcinoma, and 2 (2.94%) Hurthle cell carcinoma (Table 2).

No significant difference was observed between thyroid cancer and age (p=0.43) and thyroid cancer and sex (p=0.87).

Table 1. Comparison of cytology reports of FNA cases in thyroid nodules presented separately by two pathologists

Total	First pathologist		Result	
	Malignant	Benign		
42	7	35	Benign	Second pathologist
73	63	10	Malignant	
115	70	45	Total	

Table 2. Frequency of malignancy type in thyroid nodules reported by surgery

Type of thyroid nodule malignancy		Frequency	Percentage
PTC	PTC	54	79.41
	MPTC	7	10.29
FTC		5	7.36
Hurthel cell carcinoma		2	2.94
Total		68	100

Discussion

As already noted, thyroid nodules are common clinical findings with a prevalence rate of 4%-7% based on physical examination (1).

FNA is used as a preoperative screening test (gold standard) to identify thyroid malignancies and other cancers. Thus, it is expected to have acceptable sensitivity and specificity.

Hatamipoor et al. (2005) studied 100 specimens from candidates for thyroidectomy visiting Shahid Mofatteh Surgical Clinic, Yasuj, Iran. In this study, FNA had the sensitivity of 78±15%, specificity of 91±13%, and accuracy of 89±13% (13).

In a study titled the "Evaluation of diagnostic value of fine needle aspiration in thyroid nodule", Mirsadraei et al. (2007) examined 536 patients with thyroid nodules who visited Imam Reza Hospital, Mashhad, Iran. They reported the sensitivity, specificity, and diagnostic accuracy of FNA to be 91.5, 89.5%, and 93.7% (14).

Moreover, Bahar et al. (2012) conducted a cross-sectional retrospective study to investigate the FNA results of patients with thyroid nodules visiting Imam Khomeini Hospital, Sari, Iran, from 2003 to 2011. Studying 217 cases of thyroidectomy, they reported the sensitivity of FNA in identifying malignant thyroid nodules to be 81.2% and its specificity to be 75.1% (15).

In addition, Riazi et al. (2013) explored the correlation between FNA cytology and pathology results belonging to 198 patients undergoing thyroidectomy in university hospitals of Bushehr, Iran. They calculated the sensitivity of 53.84%, specificity of 98.01%, and diagnostic accuracy of 81.81% for thyroid FNA (16).

Furthermore, Kini et al. (2006) explored the role of FNA in managing patients with thyroid enlargement from 2001 to 2003. Based on 172 specimens, the

diagnostic power of FNA was 86.6% in Grades 0-1 thyroid cancers and 96% in Grade 2 cancers (17).

Furthermore, Mandal et al. (2011) investigated the diagnostic value of FNA for thyroid nodules in 120 patients and reported the sensitivity of 90%, specificity of 84.6%, and diagnostic accuracy of 86.1% for thyroid FNA (18).

In the study conducted by Gunaratne et al. (2016) between 2009 and 2013, the sensitivity, specificity, and accuracy of FNAC were 94.1%, 87.2%, and 90.4%, respectively (19).

Review of literature reveals different ranges for the sensitivity, specificity, and diagnostic accuracy of FNA. Sensitivity ranges from 53.84% (Riazi et al., 2013) to 91.1% (Mirsadraei et al., 2007) and specificity ranges from 75.1% (Bahar et al., 2012) to 98.01% (Riazi et al., 2013). A similar variation is observed for diagnostic accuracy. The sensitivity, specificity, and diagnostic accuracy calculated in the present study by two pathologists were different in 31% cases. However, the resulting values fell in the ranges reported by the noted studies.

Various factors, including the physician's skill in performing the biopsy and the interpretation of results by the pathologist, affect FNA results. The clinical approach to some results, including suspicious ones, is important as well. If suspicious cases are considered positive, sensitivity is increased and specificity is decreased. On the other hand, if suspicious cases are considered negative, sensitivity is reduced and specificity is increased (16).

In the present study, the agreement between the two pathologists was 69% and their diagnostic accuracy differed, indicating that, in addition to the noted factors, the pathologist's skill affects the diagnostic accuracy of FNA specimens. Furthermore, according to some researchers, nodule size affects the sensitivity but not the specificity of FNA (20).

In the present study, in terms of surgical pathology, cases of FTC, MPTC, PTC, and Hurthle cell carcinoma were 79.41, 10.29, 7.36, and 2.94%, respectively.

Fagin et al. (2016) conducted a review study on biologic and clinical nature on thyroid cancer. Results revealed that thyroid cancer consists of about 84% papillary cancer (including 33% microcarcinoma), 2%-5% follicular carcinoma, 3%-5% medullary thyroid carcinoma, 2% Hurthle cell carcinoma, 1% anaplastic cancer, approximately 6% poorly differentiated carcinoma, and 1% other cases (21). The findings of the present study are mostly consistent with the findings of Fagin et al. (2016).

According to Kenneth et al. (2015), thyroidectomy is recommended for patients with highly suspicious thyroid nodules who present specific mutations (e.g. RAS- or BRAF-positive mutations) in molecular genetic analysis. However, if no mutation is observed, the decision on thyroidectomy or monitoring the nodule depends on the clinical condition of patients. Based on this study, when FNA reports an atypia with follicular lesion of diagnostic insignificance or follicular neoplasm, nodules with the size of 1 cm or larger can be monitored without referral for surgery and thyroidectomy in case of a negative molecular analysis in terms of mutations or becoming cancerous (4). In the present study, all patients with similar FNA presentations were referred for surgery and thyroidectomy as molecular genetic analysis was not available.

Based on the noted limitations, we suggest that studies with larger sample sizes over a longer period be conducted to better estimate the sensitivity and specificity of FNA in identifying malignant thyroid nodules. Moreover, unnecessary thyroidectomies can be reduced with the help of more accurate methods, e.g. molecular genetic analysis, to diagnose thyroid malignancies (Bethesda Class 3 and 4).

Conclusion

The prevalence of thyroid cancer has markedly increased in the past decade. If performed by experienced physicians on the nodule and adequate samples are extracted and then analyzed by experienced pathologists, FNA can be employed in differentiating benign and malignant cases with a relatively high sensitivity and specificity as an inexpensive, low-risk, and easy diagnostic tool.

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