Full Length Research article

Accuracy of Fine Needle Aspiration Cytology in the Diagnosis of Thyroid Swelling compared to the Postoperative Pathology Report

Abdihakim Elmi Abdishakur; Waleed Atef Alyan*; Amr Abdelraouf Abdelnaser; Mohamed Abdel Sattar Abdel Hamid

General Surgery Department; Faculty of Medicine - Ain Shams University, Egypt.

ARTICLE INFORMATION   ABSTRACT

Thyroid nodules are common clinical lesion with a prevalence of 4 to 7% in the general population. Most are ultimately determined to be benign, but approximately 5% are malignant. Recent literature suggests that each patient with thyroid nodule should undergo a complete evaluation that includes a detailed history and examination these reports suggest that thyroid function tests radioactive scan, and ultrasonography add useful information. These measures however, cannot distinguish with certainly benign from malignant lesions. High-risk categories classically are defined by older age, male gender, history of radiation exposure, family history. The presence of a solitary, fixed" cold" hard or growing nodule, hoarseness, lymphadenopathy, nonregression with thyroid hormone treatment, and a solid or complex mass on ultrasound. Our goal was to evaluate the clinical work up of patients with thyroid nodules to correlate factors which may predict benign or malignant disease. We evaluated preoperative FNA and post-operative histopathological examination to determine relative accuracy and usefulness in guiding management of thyroid nodules. We analyzed outcomes of patients with equivocal FNA findings, e.g. "follicular" to determine the final pathologic diagnosis of these lesions. This study included 50 patients (36 females and 14 males) who were selected from those who presented to the department of general surgery at El Demerdash University Hospital and Nasr city insurance hospital during the period between September 2018 and April 2019 with either a solitary, dominant, recurrent thyroid nodules or thyroid enlargement with lymph nodes. All cases were subjected to ultrasonic examination to the thyroid gland, the results showed no definite diagnostic difference between benign and malignant lesions. The age range of the studied cases was from 16-68 years old (mean age 44.78 years). The results of Histopathological examination were Benign (39 cases) (78%), Malignant (8 cases) (16%), Atypical (3 cases) (6%). Six case was classified by FNAC as benign but proved to be malignant by histopathologic examination (false negative). The false negative rate for malignant lesion by using the FNAC in this study was 14.2%. False-negative results are generally due to large or cystic lesions, and to clinical inexperience. Nodules larger than 3 cm are more likely to cause false-negative results than smaller lesions. The face underscores the importance of obtaining several aspirates and, for lesion larger than 3 cm, even 5 aspirates, in order to ensure an adequate and representative sample. All cases with thyroid nodules should have FNAC as a pre-operative diagnostic method to reduce the number of patients referred for surgery. FNA is better done under ultrasound guidance to increase the accuracy of the results. FNAC should be done for solitary, recurrent, dominant nodules & nodules associated with lymphadenopathy because it's rather reliable method to screen such nodules. It can reach a proper diagnosis in the majority of patients. It has low false positive results & acceptably slightly higher false negative rate & a higher still rate of suspicious results. In the suspicious cases, frozen section is especially indicated as it solves the problem in 60%.

Introduction

Thyroid disorders are one of the common problems encountered in clinical practice with majority of benign in nature *(Burguera and Gharib, 2000)*. They are endemic in mountainous region of the world, where the soil, water & food supply contain little iodine *(Elahi et al., 2005)* and endemic area for iodine deficiency goiter. In many cases non-neoplastic goiter present as a solitary thyroid nodule (STN). Most of the STN are benign, few are malignant. The endemicity varies from one place to another. Nodular thyroid disease is more prevalent than diffuse goiter. Long standing goiter (more than

5 years) is regarded as a risk factor for the development of thyroid cancer *(Suohel et al., 2009)*.

Thyroid cancer is a relatively rare malignancy, representing only 1.5% of all the cancers, but it is the commonest endocrine cancer accounting for 92% of all endocrine malignancies *(Islam, 2010)*. Papillary carcinoma is the most common thyroid cancer followed by follicular, medullary, anaplastic and lymphoma. So, evaluation of thyroid swelling should be undertaken by careful history taking, physical examination and investigation like FT3, FT4 and TSH level with FNAC and

further evaluation by postoperative histopathological examination. Fine needle aspiration cytology (FNAC) is a well-established outpatient procedure used in the primary diagnosis of palpable, thyroid swelling. FNAC gained acceptance in the UK and USA in 1970 *(Niazi et al., 2007)*. Currently this technique is practices worldwide and it is the investigation of choice in thyroid swelling. The limitation includes follicular carcinoma, false negative results, false positive results and a proportion of FNAC result fall into the indeterminate or suspicious group. The sensitivity of thyroid FNAC ranges from 80 to 98% and its specificity from 58 to 100% *(Thomson, 2006)*.

FNAC is simple, cost effective, readily repeated and quick to perform procedure in the outpatient department with excellent patient compliance important factor for the satisfactory test includes representative specimen from the nodule and an experienced cytologist to interpret findings. It is often used as the initial screening test for diagnosis of thyroid nodules. Thus, to summarize, FNAC plays a useful role in the preoperative investigation of the thyroid gland diseases. The experience, as well as the skills of the cytopathologist in aspiration and interpretation, is crucial. Fine needle aspiration is a good predictor of malignancy which results in a smaller proportion of excisions for benign nodules *(Chandio et al., 2018)*.

The aim of this study is to compare accuracy of fine needle aspiration cytology in the diagnosis of solitary thyroid nodule compared to postoperative histopathological examination of the removed gland. Identical results will probably save many patients unnecessary thyroidectomies.

Patients and methods
Patients
This study Included 50 patients (36 females and 14 males) who were selected from those who presented to the department of general surgery at El Demerdash University Hospital and Nasr city insurance hospital during the period between September 2018 and April 2019 with either a solitary, dominant, recurrent thyroid nodules or thyroid enlargement with lymph nodes.

Patients were enrolled in the study according to the following criteria: No clinical evidence of hyperthyroidism, patients age above 18, patient of both sexes presented with thyroid swelling, patients who underwent (FNA) fine needle aspiration cytology before surgery, and Patients who underwent thyroid surgery followed by histopathological examination (paraffin section).

Methods
All the patients included in study were subjected to the following: Full history taking and clinical examination with special emphasis on detection of thyrotoxic or malignant cases. Laboratoryinvestigation: include preoperative routine investigation with special emphasis on thyroid function tests and detection of serum calcium and phosphorus to exclude thyrotoxic cases or cases with parathyroid affection. Neckultrasonography: to differentiate cystic thyroid lesions from solid ones and to detect with multiple nodules that felt clinically as solitary thyroid nodule. Indirect laryngoscopy: to assess the condition of the vocal cords. Fine needle aspiration cytology: was performed as described by *(Obaid and Auti, 2017)*. With a 20-gauge needle and approximately at least two slides for each aspiration, which were stained by heamotoxyline and eosine.

In this study, fixation was done immediately by immersion in 95% ethyl alcohol, and stained with Papanicolaou stain as ethyl alcohol is universally accepted as best fixatives for Papanicolaou stain. And this method is very helpful for diagnosing follicular lesion and for evaluation of most others since excellent nuclear details are demonstrated *(Gharib et al., 2010)*.

Smears were classified into the following categories:
A- Unsatisfactory: Marked hypo-or a cellular aspirate or aspirate containing degenerated cellular material.
B- Benign: The Presence of group of uniform follicular cells without colloid material. The presence of large amount of colloid in the background was usually regarded as a sign of benign process.
C- Suspicious (indeterminate): Include smears that contained cells exhibiting minimal deviation from the benign pattern including slight nuclear pleomorphism or infrequent prominent nucleoli together with prominent follicular arrangement, so the differentiation can be made cytologically
D- Malignant: These smears were usually cellular and the cells showed definite malignant criteria *(Tamhane et al., 2016)*.
   1. Histopathologic examination: All operative specimens were fixed in 10% aqueous solution of formalin for at least 24 hours. Paraffin blocks were done Histopatholgic examination of all cases was done without previous knowledge of the cytologic diagnosis. (Conventional criteria for thyroid lesions were applied).

A correlation was established between the cytologic findings and the post-operative histopathologic findings, and the following parameters were analyzed.
1- Sensitivity: the proportion of patient with malignant thyroid disease and positive cytologic finding.
2- Specificity: the proportion of patients without malignant thyroid disease and negative cytologic finding.
3- False-positive fraction: the probability of positive cytologic finding in patient without malignant thyroid disease.
4- False-negative fraction: the probability of negative cytologic finding in patient with malignant thyroid disease.
5- Positive predictive value: the probability of having malignant thyroid disease and positive cytologic finding i.e. percentage of correct positive diagnosis.
6- Negative predictive value: the probability of giving benign thyroid disease and negative cytologic findings i.e. percentage of correct negative diagnosis.
7- Accuracy index: the proportion of correct result (true positives and true negatives) in relation to all cases studied *(Sikder et al., 2012)*.

Statistical Analysis
Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The comparison between groups regarding qualitative data was done by using Chi-square test. Receiver operating characteristic curve ROC) was used in the qualitative form to determine sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of FNAC by taking POH as a gold standard. The confidence interval was set to 95% and the margin of error accepted was set to 5%.

Results

Table (1): Sex and age distribution of the studied cases

		No. = 50
Age	Mean±SD	44.78 ± 12.43
	Range	16 – 68
Sex	Female	36 (72.0%)
	Male	14 (28.0%)

Table (2): FNA and POH results of the studied cases

		No.	**%**
FNAC	Benign	42	84.0%
	Malignant	2	4.0%
	Suspicious	6	12.0%
POH	Benign	39	78.0%
	Malignant	8	16.0%
	Atypical	3	6.0%

Table (3): Predictive value of the FNA comparison with POH

FNAC	**POH**						**Test value***	**P-value**	**Sig.**
	Benign		**Malignant**		**Atypical**				
	No.	**%**	**No.**	**%**	**No.**	**%**			
Benign	34	87.2%	6	75.0%	2	66.7%			
Malignant	0	0.0%	1	12.5%	1	33.3%	10.073	0.039	S
Suspicious	5	12.8%	1	12.5%	0	0.0%			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*:Chi-square test

Table (4): Accuracy of FNA, sensitivity and specifity comparison with POH

FNAC		**POH_A**				**Test value***	**P-value**	**Sig.**
		Benign		**Malignant**				
		No.	**%**	**No.**	**%**			
FNAC	Benign	41	100.0%	6	66.7%			
	Malignant	0	0.0%	3	33.3%	14.539	0.000	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*:Chi-square test

Parameter	**Accuracy**	**Sensitivity**	**Specificity**	**PPV**	**NPV**
FNAC	88.0	33.3	100.0	100.0	87.2

Sensitivity = TP
Specificity = TN
PPV = TP / Total positive (TP + FP)

NPV = TN / Total Negative (TN + FN)
Accuracy = (TP + TN) / Total no. of patients

Discussion

Fine needle aspiration cytology is regarded as the gold standard initial investigation in the diagnosis of thyroid swellings. The technique is safe, simple and quick with low complication rates. Several other tests such as high-resolution ultrasonography, radioisotope scanning and FNA biopsy have been used for evaluation of thyroid swellings before proceeding to thyroid surgery. Studies have demonstrated that among all these diagnostic modalities FNAC is the most accurate and cost-effective screening test for rapid diagnosis of thyroid swellings *(Hirachand et al., 2013)*. In, this discussion accuracy of FNAC in the diagnosis of thyroid swelling compared with concluded results with some of the available international studies. Results of this study are almost similar to that of the international studies *(Sikder et al., 2012)*. In this study all cases were subjected to ultrasonic examination to the thyroid gland, the results showed no definite diagnostic difference between benign and malignant lesions, the main value of ultrasonic examination to the thyroid gland was to differentiate between cystic, solid, and mixed nodules and also

diagnose multinodular goiter presenting with solitary thyroid nodule. Aspiration under ultrasound guidance is now widely used particularly for small nodules deep in the neck, and it contributes to diagnostic accuracy *(Hatatdat et al., 1998)*. In this study the results of the FNAC were: benign 84% (42 cases), malignant in 4% (2 cases), suspicious in 12% (6 cases).The two cases (4%) classified as malignant by FNAC in this study were diagnosed by histopathologic examination as Atypical follicular lesion and nodular goiter for immuno-histochemistry in one, papillary carcinoma in the other one. In the 6 cases (12%) classified as suspicious by FNAC in this study were diagnosed by histopathologic examination as Malignant Follicular variant of papillary carcinoma with Hashimoto thyroiditis in one, Benign Hurthle cell neoplasm in one, and benign nodular goiter for 4 cases which agrees with *Sharma et al. (2017)*. On cytology of 11 (5.5%) patients with indeterminate lesions, follicular neoplasms, and hurthle cell neoplasms were diagnosed in 3% and 2.5% patients, respectively. In the 42 cases (84%) classified as benign by FNAC in this study were diagnosed by histopathologic examination by Atypical follicular lesion for immune-

histochemistry in one case, malignant follicular carcinoma in three cases and Malignant Papillary carcinoma in three cases. In this study the results of the Histopathological examination were Benign (39 cases) (78%), Malignant (8 cases) (16%), Atypical (3 cases) (6%). Six case was classified by FNAC as benign but proved to be malignant by histopathologic examination (false negative). The false negative rate for malignant lesion by using the FNAC in this study was 14.2%. False-negative results are generally due to large or cystic lesions, and to clinical inexperience. Nodules larger than 3 cm are more likely to cause false-negative results than smaller lesions. The face underscores the importance of obtaining several aspirates and, for lesion larger than 3 cm, even 5 aspirates, in order to ensure an adequate and representative sample.

Which agrees with *Sikder et al. (2012)* in his study 8 were false negative (which was non neoplastic on FNAC but were malignant on paraffin section). And also with *(Sharma et al., 2017)*. The negative predictive value was 78.94% which was lower than other studies because there were four false negative cases in our study. False-positive rate in this study was zero which agrees with *Chandio et al. (2018)* who reported a false-positive diagnosis indicates that a patient with a malignant FNA result was found on histologic examination to have benign lesions. False-positive rates vary from 0% to 8% (average, 3%).In this study, the benign lesion classified by FNAC were 42 cases (84%), and the postoperative histopathologic examination was 39 cases (78.6%). The accuracy of FNA comparison with POH was 88% and the sensitivity was 33.3% and the specificity 100%. The positive predictive value was 100% and negative predictive value was 87.2 %.Which agrees with *Sikder et al. (2012),* overall sensitivity of FNAC were 68.75%, specificity 100.00% and accuracy 90%; PPV=100% & NPV=87.18%. And also agrees with *Hirachand et al. (2013),* statistical analysis of our data shows the diagnostic accuracy of FNAC to be 95.7%. Fine needle aspiration cytology showed a sensitivity of 96.4% and a specificity of 94.4%.The major reason for the wide range of sensitivity and specificity ratios is the differences in the categorization of lesion, some authors categorize follicular lesions as histopathological benign, while others categorize these lesions as malignant *(Chandio et al., 2018)*. And in this study the suspicious and atypical results categorized as same as the result of the other side benign or malignant.

The positive predictive value in this study was 100% that agrees with *Sharma et al. (2017)*. The positive predictive value was 100% in our study which was higher as compared to other studies because we did not report even a single case as false positive. FNAC is now considered as the diagnostic test of choice for the preoperative evaluation of thyroid lesions and selection of patients for thyroid surgery. It is a simple, inexpensive, safe, rapid, minimally invasive, and can be carried out in outdoor patients with excellent patient compliance and considered to have a high sensitivity and specificity. However, it has some limitations in specimen adequacy, sampling technique, skill, and experience of pathologist and inability to distinguish follicular lesions reliably, which includes hyperplastic nodule in goiter, follicular neoplasms and papillary carcinoma (follicular variant).

It is rarely associated with complications such as hematoma, massive intrathyroid hemorrhage, necrosis, and local metastasis of malignancy *(Sharma et al., 2017)*.

Conclusion

All cases with thyroid nodules should have FNAC as a pre-operative diagnostic method to reduce the number of patients referred for surgery. Fine needle aspiration cytology is better done under ultrasound guidance to increase the accuracy of the results. FNAC should be done for solitary, recurrent, dominant nodules & nodules associated with lymphadenopathy because it's rather reliable method to screen such nodules. It can reach a proper diagnosis in the majority of patients. It has low false positive results & acceptably slightly higher false negative rate & a higher still rate of suspicious results. In the suspicious cases, frozen section is especially indicated as it solves the problem in 60%.

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