Diagnostic value of Fine Needle Aspiration Cytology of Thyroid Nodules: Experience at King Hussein Medical Center

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ABSTRACT

Objective: To evaluate the diagnostic accuracy of fine needle aspiration cytology in comparison to histopathological findings in patients with Thyroid Nodules.

Methods: This study carried out at King-Husain Medical Center (Royal Medical Services) from February 2012 to September 2013. Records of 103 patients treated surgically for thyroid nodules were reviewed. The patients who had pre operative fine needle aspiration cytology as first line of the evaluation and the final post operative histopathology report available were included in the study. All cases underwent surgery and histopathology results were compared with the cytology results. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were calculated.

Results: Of the103 patients, 83 female 80.6%, 20 male 19.4%. The cytological diagnosis was made according to following categories: Benign, Suspicious, Malignant and Inadequate sampling. Among 40 "Benign cases", 37 were benign and 3 turned out to be malignant. Among 38 cases from "suspicious, 8 were benign and 30 were malignant. Out of 21 patients from "Malignant" group, 19 were malignant and 2 were benign. Among four patients from the "Inadequate sampling group", 3 turned out to be benign and one was malignant. The overall results showed a sensitivity of 92.4%, specificity of 80%, and positive predictive value of 83.1%, negative predictive value of 90% and diagnostic accuracy of 86.4%.

Conclusion: Fine needle aspiration cytology is a minimally invasive procedure, simple, reasonable approach and the preferred initial diagnostic test in all patients with thyroid nodule. Fine needle aspiration cytology has high sensitivity in picking up malignancy in thyroid and also has high diagnostic accuracy in the evaluation of thyroid nodules and we should improve specificity.

Key words: FNA accuracy, Histopathology, Thyroid nodules.

Introduction

  The thyroid gland is unique among endocrine glands in that it is the first endocrine gland to appear in the fetus, arise from the fourth branchial pouch. It is the largest of all endocrine glands (weighing about 25g) and is the only one which is amenable to direct physical examination because of its superficial location.

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Thyroid nodules are very common problem in clinical practice. The estimated prevalence of palpable thyroid nodules in the general population is approximately 4% to 7%, but incidental finding of nodules by thyroid ultrasound suggest a much higher prevalence, ranging from 19% to 67%.[1,2] With a much higher rate in areas of iodine deficiency and in people exposed to radiation. Increasing age and female gender also seem to increase the risk of the development of thyroid nodules. Thyroid nodules, usually benign; only about 5% of these nodules harbor malignancy. Biopsy of a thyroid nodule is commonly done to rule out thyroid cancer. Fine-needle aspiration biopsy is a safe, out-patient technique and the single most important procedure for differentiating benign from malignant thyroid nodules and to take a decision 5 for treatment plan (surgery or conservative). Fine Needle Aspiration Cytology (FNAC) has limitations which include false negative results, false positive results, and suspicious or indeterminate results.[3]

Our aim of this study was to evaluate the accuracy of FNAC findings in correlation with histological findings in patients underwent thyroidectomy for any reason in our surgical unit.

Methods

This retrospective study include data (collected from patients medical records) of all the patients who underwent thyroid surgery either for malignant, cosmetic or compression reasons at King Husain Medical Center (KHMC) from February 2012 to September 2013. The study includes 103 patients with clinically palpable thyroid nodules. Thyroid function test including free thyroxin, free triiodothyronine, and thyroid stimulating hormone were initially performed followed by FNAC of thyroid nodules which carried out by pathologists as outpatient procedure.

The aspiration technique was the standard one described in literature, using a 23-gauge needle. Smears were immediately fixed with 95% ethyl alcohol solution, and staining was performed using Papanicolaou, Hemacolour®, and Haematoxylin and Eosin (H and E) stain. In cases of cystic lesions, the cyst contents were evacuated and smears were prepared from the cyst fluid and re-aspiration was performed if any solid mass palpable.[4,5]

Cytology results were categorized into four groups, benign, suspicious, malignant and unsatisfactory. The histopathology results were classified as either benign or malignant.

Pre-operative FNAC results were then compared with the definitive histological diagnosis. Those cases which were found to be malignant by cytology as well as by histology were labelled as True Positive (TP). False positive (FP) were those diagnosed as malignant on cytology and turned to be benign on histology. True negative (TN) were benign on both cytology and histology. False negative (FN) were negative on cytology but positive for malignancy on histology. The diagnostic accuracy was calculated as:

- Sensitivity= True positive X 100 / True Positive + False Negative
- Specificity= True Negative x 100 / True Negative + False Positive
- Negative Predictive Value= True Negative X 100 / False Negative + True Negative
- Positive Predictive Value= True positive x 100 / False Positive + True Positive
- Accuracy= True Positive + True Negative x 100 / True Positive + False Positive + True Negative + False Negative

We assessed the accuracy of FNAC findings by comparison to the final histology of the thyroidectomy specimen as the gold standard for the diagnosis.

Results

A total of 103 patients had thyroid swellings undergone FNAC and subsequent thyroid surgery during the study period from February 2012 to September 2013. Eighty three 83 (80.6%) females, 20 (19.4%) males with female to male ratio 4.2:1. Age of population studied ranged between 14 to 86 years with a median of 43 years. FNAC results were interpreted as Inadequate, benign, suspicious and malignant (Table I). These results compared with post operative findings (Histopathology) Table II. FNAC has a sensitivity of 92.4%, specificity of 80%, and positive predictive value of 83.1%, negative predictive value of 90% and diagnostic accuracy of 86.4% (Table III).

Table I: Distribution of cases according to cytological diagnosis

Cytological diagnosis	No.	%
Benign	40	38.8
Suspicious of malignancy	38	36.9
Malignant	21	20.4
Inadequate	4	3.9
Total	103	100%

Table II. Correlation of FNAC with histopathological diagnosis

Histopathology Diagnosis	FNAC				Total
	Benign	Malignant	Suspicious	Inadequate	
Benign	37	2	8	3	50
Malignant	3	19	30	1	53
Total	40	21	38	4	103

Table III: Statistical analysis

True negative (TN)	40
True positive (TP)	49
False negative (FN)	4
False positive (FP)	10
Sensitivity	92.4%
Specificity	80%
Positive predictive value (PPV)	83%
Negative predictive value (NPV)	90%
Accuracy	86.4%

Discussion

Thyroid nodules are common, the vast majority of nodules are benign, the main concern is to exclude the possibility of thyroid cancer and to avoid unnecessary surgery and it's complications.[6] Several tests have been used for evaluation of thyroid nodules to distinguish benign from malignant nodules and before proceeding to thyroid surgery such as Thyroid ultrasound, radioisotope scanning and FNA biopsy. Studies have demonstrated that among all these diagnostic modalities, Fine needle aspiration cytology has been advocated as the 1st investigation of choice when assessing thyroid nodules. The procedure is relatively simple, cheap, most accurate and with few complications.[7]

The accuracy of the FNAC analysis approaches 95% in the best centers as regards differentiation of benign from malignant nodules of the thyroid. The sensitivity ranges from 65% to 98% and the specificity from 72 to 100%. In our study, the analysis of the data revealed a sensitivity of 92.4% and specificity of 80%, which translates into a diagnostic accuracy of 86.4%. The

sensitivity, specificity, accuracy, PPV, and NPV in our study are comparable with other studies from different parts of the world.[7,8]

We use the simplified four-category system for FNAC results which include Inadequate, Benign, Suspicious, and Malignant. However; The Bethesda system recommends categorisation of results into six categories; I: inadequate; II: benign; III: atypical follicular cells of undetermined significance (FLUS); IV: follicular neoplasm (FN); V: suspicious for malignancy; and VI: malignant. Some researchers using this system have found considerable overlap in the categories. As most of the benign conditions can be managed medically, it saves the patient from unnecessary surgery. In our study the 103 patients undergone surgery according to, clinical findings suggesting the diagnosis of thyroid carcinoma, cytologically suspicious or malignant diagnosis. However, compression symptoms or cosmetic reasons may also be the reason for surgery.[9,10]

False negative FNAC results are expected in FNAC diagnosis of atypical cell, follicular or Hurthle cell lesions should be advised to undergo

surgery, as a significant proportion harbour malignancy. Inadequate sampling, which gives rise to non-diagnostic results. Insufficient cellular material from cystic or haemorrhagic lesions, the skills of the operator as well as the interpreter in performing aspirations, the numbers of punctures, and the technique of preparing smears. In our study we can calculate the true frequency of false negative results, because all patients with benign cytological findings undergo surgery. The true false negative rate (the percentage of patients with benign cytology in whom malignant lesions are later confirmed on histopathology and calculated as False Negative X 100 / False Negative + True Positive) which ranged from 1% to 16% in different series. In our study, four false negative cases were found with a rate of 7.5%.[10,11]

The inadequate samples or non diagnostic result is one of the limitations of this procedure. Unsatisfactory rates are more variable depends on the skill of the aspirator, number of passes, and the skill of the cytopathologist interpreting the sample. The rate of malignancy found in operated cases with non-diagnostic FNAC varies widely between studies ranging from 2.2% to 51%. Use of ultrasound guidance was shown to decrease the proportion of non-diagnostic results as compared to freehand FNAC, the risk of malignancy declines with each successive repetition of non-diagnostic FNA. This would suggest a possible role for observation in patients who have had three or more non-diagnostic FNAC results and there is no clinical suspicion of malignancy. The rate of inadequate samples is 1-5%, in our study four cases reported as inadequate with a rate of 3.9% considered negative for malignancy on cytology one case out of four reported malignant on histopathology 25%.[11-13]

The false positive rate (FPR) indicates that a patient with malignant FNAC result was found on histological examination to have benign lesion. The false positive rate (FPR) was 20% in our study, which calculated as False Positive X 100 / False Positive + True Negative. However, this is expected for FNAC of the thyroid as a large group falls in the category of malignant and suspicious or consistent with follicular neoplasm, out of which a significant number turn out to be follicular adenomas or hyperplastic /

adenomatous nodules. While evaluating our results not only all cases reported as malignant 21 case 20.4% on cytology, two 9.5% turn out to be benign on histopathology (FP), and those reported as suspicious for follicular neoplasm, papillary carcinoma or other malignancy were considered positive, with a total of 38 case 36.9% on cytology, 8 cases 21.1% turn out to be benign on histopathology (FP). Which is true concerning FNAC results because of its inability to distinguish between benign and malignant follicular lesions, Hurthle cell lesions and Lymphocytic lesions in the absence of nuclear features of papillary carcinoma and overlapping features of hyperplastic nodules and follicular neoplasm, another limitation of FNA cytology. This was because all the above need further surgical management.[13-15]

In our study FNAC has a sensitivity of 92.4%, specificity of 80%, and positive predictive value of 83.1%, negative predictive value of 90% and diagnostic accuracy of 86.4% which is useful to reassure patients with thyroid nodules according to NPV 90%, and on the same time pay attention to FNAC pitfalls and clinical picture of the patients.

Conclusion

Fine-needle aspiration cytology (FNAC) is simple, cheap, with few complications and has an essential role in the evaluation of patients with thyroid nodules. It reduces the rate of unnecessary thyroid surgery for patients with benign nodules and appropriately triages patients with thyroid cancer to appropriate surgery. With current thyroid FNA practice, the percentage of resected nodules that are malignant more than 50%.The possibility of false negative results because of sampling error, must kept in mind and these patients should be followed up.

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