

Diagnostic Role of Fine Needle Aspiration Cytology in the Diagnosis of Solitary Thyroid Nodules in Pakistan – A Comparative Study

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ABSTRACT

An analysis of management of 50 patients with thyroid swellings who presented in the outpatient department of Mayo Hospital Lahore is made. Main aim of the study was to establish the role of fine needle aspiration cytology in the diagnosis and management of solitary or dominant thyroid nodules. Evaluation of results obtained is done and comparison with other studies made. In our study 3 patients were male and 47 were female. The definitive management of these patients mainly depends upon the histological or tissue diagnosis. The two methods used to obtain the tissue diagnosis are histopathology and Fine needle aspiration cytology. For histopathology we have to remove the nodule first and the problem with this method is that if the nodule turns out to be malignant, we have re-do the surgery to complete the procedure. In fine needle aspiration cytology we can have the tissue diagnosis before hand and do the definitive and complete procedure in the first go. In our study the sensitivity, specificity and diagnostic accuracy of FNAC was calculated in comparison with the surgery and histopathology as gold standard in Pakistan.

Key words: FNAC, solitary thyroid nodule

INTRODUCTION

Fine needle aspiration cytology is becoming an integral part of selected patient management but comprises only a part of the overall evaluation. Fine needle aspiration cytology is now recommended as the first choice for the evaluation of palpable thyroid nodules internationally suggesting that FNAC is an effective and accurate technique for the diagnosis and further management of palpable thyroid nodules¹.

The commonly used procedure for the diagnosis of thyroid nodule malignancy is based on high resolution thyroid ultrasonography (US) combined with US-guided fine needle aspiration cytology (FNAC). With the advent fine-needle aspiration cytology (FNAC), the role of frozen section (FS) in the management of non-toxic thyroid nodules has become uncertain². A correct classification of the carcinoma type on the basis of FNAC was possible only in 69% patients³. Being a cost-effective technique and having the capacity to provide exact morphological diagnosis in a large variety of thyroid lesions, cytology is obviously the method of choice in assessment of thyroid nodules⁴.

Histopathological evidence of malignancy was found in 10% of patients and papillary carcinoma was heading the list⁵. To see the impact of FNAC in the

management of thyroid nodules FNAC was found highly sensitive in detecting malignancy in solitary thyroid nodules⁶. A major advance in the diagnosis of thyroid nodules has been achieved with the perfection and common use of fine needle aspiration cytology which can obviate a lot of unnecessary surgery in thyroid lesions⁷. There are no early clinical symptoms and signs of investigations which can differentiate between benign and malignant conditions except fine needle aspiration cytology which is reliable diagnosis test and is helpful in subsequent management of these patients⁸. This study was designed to highlight the role of FNAC in definitive diagnosis and management of clinically palpable solitary thyroid nodules.

Operational definition: Thyroid nodule is a discrete swelling in an otherwise impalpable gland is termed isolated or solitary nodule. Dominant nodule is a similar swelling in a gland with clinical evidence of generalized abnormality in the form of palpable contra lateral lobe or generalized mild nodularity.

FANC Procedure: Patient lies in supine position with neck extended. No anesthesia usually required. Skin is cleaned with antiseptic solution. Under aseptic measure swelling is fixed with one hand and other hand is used to introduce needle into the swelling. When the tip of needle is in the centre of the lesion to be sampled negative pressure is applied. The needle moved to and fro in different angles of nodule to get the tissue detached. Then the needle is withdrawn while negative pressure being applied. The needle

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separated and about 0.3cc air sucked. Needle is reattached and material is expressed on glass slides. It is dried in air and then fixed with alcohol for ½ to 1 minute. Then gimsa stain is put on slide for 1-2 min and then washed with tap water. After that reading of slide under microscope is done.

Diagnostic accuracy of FNAC was assessed by comparing the results of FNAC with surgery and histopathology as gold standard. The sensitivity, specificity and diagnostic accuracy of FNAC was calculated.

MATERIALS AND METHODS

This was Comparative Study carried out at the Department of Surgery, (East Surgical Ward), Mayo Hospital, Lahore. Fifty patients of thyroid nodules were included. Duration of the study was six months from 3rd February 2007 to 3rd August 2007. The objective of this study was to assess the diagnostic accuracy of fine needle aspiration cytology in thyroid nodular disease. Sampling technique was convenience non-probability sampling. Inclusion Criteria were age between 12 to 60 years, both sexes and patients presenting with swelling arising from any lobe of thyroid. Exclusion criteria included patients with confirmed diagnosis other than thyroid nodules i.e. puberty goiter, grave's disease, multi nodular goiter etc. and patients with advanced fixed thyroid tumors.

All patients included in the study were selected from outpatient department of East Surgical Ward, Mayo Hospital Lahore. Informed consent from all patients included in the study was taken. After admission in the ward all patients were recorded for their demographic features i.e. age, sex, address, occupation etc. Presenting complaints and detailed history of present illness were recorded. Clinical examinations as per Performa were recorded. All routine investigations i.e. blood complete examination, blood sugar, urea, creatinine, x-ray chest, ECG, complete urine examination, blood grouping and cross matching and thyroid function tests (T3, T4, TSH), thyroid scan, indirect laryngoscopy were done. Then the procedure of FNAC was carried out. The cases were operated and specimens sent for histopathology. The diagnostic criteria were histopathology reports. Data analyzed with the help of SPSS version 10. Numerical variables i.e. age and results of lab investigations (Hb%, Blood sugar, Thyroid functions tests etc) were presented as frequencies, means, and standard deviation. The quantitative variables like lab investigations were applied "T-test". The qualitative data i.e. results of FNAC and histopathologies were subjected to Chi-square test. The table for calculating

the sensitivity, specificity and diagnostic accuracy was drawn as 2x2 tables and analyzed.

RESULTS

This study was conducted on 50 patients (males and females from the age of 12-60 years). Thyroid nodule (solitary and dominant) were diagnosed clinically over a period of six months, in East Surgical Ward with the collaboration of other surgical units of Mayo Hospital, Lahore and pathology department King Edward Medical University, Lahore.

Ages of the patients ranged from 12 to 60 years with mean age 35.60±13.19. The highest numbers of patients were aged between 21-30 years i.e. 19 (38%). Four patients (8%) were aged between 12-20 years. 13 patients (26%) were aged between 31-40 years. Five patients (10%) were aged between 41-50 years, while nine patients (18%) were of age between 51-60 years. Out of 50 patients 47 (94%) were female and only three (6%) were males. Male to female ratio was 1:15.6. Five patients (10%) showed symptoms of pain. Seven patients (14%) showed pressure symptoms while there were no symptoms in 38 patients (76%). Regarding site of swelling, there were 18 patients (36%) had swelling at right side, nine patients (18%) at middle of neck and 23 patients (46%) had swelling at left side. Eleven patients (22%) had small size of nodule (< 2 x 2 cm approximately). 32 patients (64%) had intermediate (2 x2 cm – 6x2 cm approximately) and only seven patients (14%) had large size of nodule (> 6x 6 cm). Ovoid shape of nodule was observed in 18 patients (36%) while hemispherical was noted in 32 patients (64%).

Out of 50 patients 26 were diagnosed as colloid nodules, 7 were diagnosed malignant and 17 were in determinant. Out of 17 cases of in determinant FNAC, 2(4%) were males and 15 (30%) females. Comparison of histopathology showed that there was no case of indeterminate. Three male patients (6%) and 40 females (80%) were benign, while seven females (14%) were malignant. Out of 43 cases of benign (histopathology), colloid goiter was observed in one male (2.32%), and it was found in 23 females (53.48%). Follicular adenomas were in two males (4.65%) and in 15 females (34.88%). Diffuse hyperplasia noted in two females (4.65%). Out of seven malignant cases (histopathology), papillary carcinoma was observed in four females (57.14%), Follicular carcinoma in two females (28.57%) and anaplastic carcinoma found in one female (14.28%).

After comparison of results of FNAC with histopathology overall sensitivity of FNAC was found 71.42% and specificity 95.34%, while positive predictive value (PPV) was 71.42% and negative

predictive value (NPV) was 95.34%. The overall accuracy was 92%.

DISCUSSION

Fine needle aspiration cytology (FNAC) is a well-established technique for pre-operative investigation of thyroid nodule⁹. The technique is one of the least invasive, cost effective and efficient methods of differentiating benign and malignant thyroid nodules^{10,11}. Many investigators have shown that FNAC is the single most sensitive, specific and cost-effective method in the investigation of solitary cold thyroid nodule^{12,13}. FNAC of the thyroid is gaining popularity among the pathologists and clinicians in all over the world.

In a study in Saudi Arabia the mean age was 36.17 ± 12.3 years (range 15-67 years) which are very close to our study.

In this study, the male female ratio is very high as compared to the other studies in Pakistan and elsewhere. Out of 50 patients in our study, 47 (94%) were females and only 3 (6%) were males. Male to female ratio was 1:15.6. The difference being highly significant ($P < 0.001$). These results are contradictory to Hussain et al, who found male to female ratio to be 1:6.9¹⁴.

Clinically 5 patients (10%) showed symptoms of pain. 7 patients (14%) showed pressure symptoms while the remaining 38 patients (76%) were symptomless. 18 patients (36%) had swelling on the right side, 9 patients (18%) had swelling in the midline and 23 patients (46%) had swelling on the left side. Eleven patients (22%) had small size of nodule ($< 2 \times 2$ cm approx.), 32 patients (64%) had intermediate ($> 2 \times 2$ cm to $< 6 \times 6$ cm approx.) and only 7 patients (14%) had large sized nodule ($> 6 \times 6$ cm).

In our study 17 (34%) cases were diagnosed as follicular lesions on FNAC, 8 (47.05%) of which were benign, 7 (41.18%) were follicular neoplasm and 2 (11.6%) uncommitted due to sampling error. When these results of FNAC were compared with findings of histopathology there were four colloid goiters, 12 follicular adenomas and 1 papillary carcinoma and no one was undetermined. These findings are highly significant and it is the pitfall of FNAC.

When the results of FNAC for colloid goiters were compared with histopathological findings, 20 cases were actual colloid goiters, while 5 were follicular adenomas and one was diffuse hyperplasia, however statistically no significant pitfall was found in this group.

In 43 histological diagnosed benign cases, there were 24 colloid goiters, with one male (2.32%), and 23 females (53.48%). Follicular adenomas were found in two males (4.65%) and in fifteen females

(34.88%). Diffuse hyperplasia was noted in two females (4.65%). On FNAC there were 26 cases of benign thyroid lesions when compared with the results of histopathology (43 cases) the difference was significant.

Comparison of malignant cases diagnosed on FNAC and histopathology was same. In our study out of 7 malignant cases (FNAC), papillary carcinoma was observed in 3 females (42.85%), anaplastic carcinoma in one female (14.28%) and suspicion of malignancy noted in one female (14.28%). Suspicion of malignancy was noted in two females (28.57%) when these results were compared with their histopathology, only two cases were found to be benign (one HCA and one hyperplasia). The difference between the results was not significant. Out of 7 malignant cases (histopathology), papillary CA was observed in four females (57.14%), follicular CA in 2 females (28.57%) and anaplastic CA found in 1 female (14.28%).

FNAC is a sensitive and highly specific method of evaluating thyroid nodules for malignancy^{(15), (16)}. After comparison of our results of FNAC with histopathology, overall sensitivity and specificity of FNAC was found 71.42% and specificity 95.34%, while positive predictive value (PPV) was 71.42% and negative predictive value (NPV) was 95.34%. The overall accuracy was 92%. Our results are consistent with the results of other studies. In a review on FNAC of the thyroid nodule, it was reported to have sensitivity ranges from 65-98% and a specificity of 72-100%¹⁷. In another study the analysis of data revealed the sensitivity of 88.9% and specificity of 96.1%, which translate to an accuracy of 94.2%. This shows that FNAC is more specific than sensitive in detecting thyroid malignancy and therefore its use as reliable diagnostic test cannot be over emphasized¹⁸.

The false negative rate (FNR) is defined as the percentage of the patients with benign cytology in whom malignant lesions are later confirmed on thyroidectomy. In reference to some authors our results about false positive and false negative are consistent with the published guidelines of the Papanicolaou society of cytopathology. The guideline suggested a false negative and false positive rate of $< 2\%$ and $< 3\%$ respectively should be achieved¹⁹. In series of studies FNR was reported ranging from 1.5 to 11.5%^{20,21}. Ashcraft and van Herle noted that FNR results varied in report series from 2% to 50% and that among 1330 patients all of whom had a histopathological examination, FNR was 1.7%⁽²²⁾. Campbell and Pillsbury et al⁽²³⁾ analyzed combined data from 912 patients with benign cytological results who had histological examination and found an FNR between 0.5% and 11.5% with a

pooled rate of 2.4%. In our series we reported two cases as false negative which translated to 4% FNR. These two cases were however confirmed histologically as follicular carcinoma and papillary carcinoma. Our value is consistent with other studies of Boey and colleagues¹⁵ and Grant and colleagues¹⁶.

The False Positive Rate (FPR) indicates that a patient with malignant FNAC result was found on histological examination to have a benign lesion. Caruso and Mzzaferri et al reported less than 6% FPR while Campbell and Pillsbury reported a rate of 1.2%. In our series we reported 2 cases as malignant but turned out to colloid goiter and diffuse hyperplasia. The FPR is 4% which agreed with the other series¹⁷ that range from 0 to 8%. The two suspicious cases in our study revealed hypercellularity with some atypia, which raised an index of malignancy.

The overall accuracy for cytological diagnostic was 92% which agrees with other studies of 95%. However the interpretation error from this study can be reduced if aspirate were obtained from different portions of the nodules as expert cytopathologists to review and interpret the slides the use of ultrasound guided FNA procedure and the use of immunohistochemical and genetic markers.

CONCLUSION

As thyroid is easily accessible, superficial mass, its fine needle biopsy is a simple and minimally invasive procedure. It is an ideal first line diagnostic test. Solitary nodule is the most important target of FNAC. FNAC provides a more rapid, safe and accurate diagnosis of solitary thyroid nodule than any other combination of clinical and laboratory tests. It allows the surgeon to do a more definitive procedure in the first surgery rather than doing an excision first and then doing the completion surgery in case of malignant lesion of thyroid.

In conclusion, FNAC of the thyroid nodules is sensitive accurate and the initial investigation of thyroid diseases in our tertiary care hospitals. We encourage our clinicians to embrace this procedure in the management of the patients.

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