Diagnostic Accuracy Of Fine Needle Aspiration Cytology In The Diagnosis Of Thyroid Lesions
S Gulia, M Chaudhury, E Sitaramam, K Reddy

Citation

Abstract

Objectives :
(1) to study the cytological features in thyroid lesions (2) to correlate the cytological and histopathological observations in thyroid lesions, whenever possible (3) to assess the diagnostic accuracy of aspiration cytology as a pre-operative screening tool

Methods :
This was a retrospective study to find the utility of fine needle aspiration cytology in thyroid lesions conducted at Maharajahs Institute of Medical Sciences, Vizianagaram. Fine needle aspiration specimens from 140 patients between January 2008 and December 2010 with thyroid swelling were analysed. Smears were stained with papanicolau stain and haematoxylin and eosine stain. The smears were classified into categories like benign, suspicious/indeterminate, malignant and unsatisfactory. Cytological diagnosis was correlated with the histopathology report wherever possible.

Results:
Of the total cases the non-neoplastic category constituted the majority of the cases (82.85%). These cases included colloid goiter, colloid goiter with haemorrhage, colloid goiter with cystic degeneration, thyroiditis, thyroglossal duct cyst and hyperthyroidism. Neoplastic lesions constituted 15.72% of all cases and included follicular neoplasm and papillary carcinoma. 52 cases underwent surgery and biopsy report was correlated with the cytological diagnosis. The overall sensitivity of the study was calculated to be 90.0%; specificity 100%; positive predictive value 100%; negative predictive value 90.5%; and diagnostic accuracy of 92.3%.

Conclusions:
FNAC is considered as an invaluable and minimally invasive, simple, cost-effective, easily repeated procedure for pre-operative screening in the non-operative diagnosis for most of the thyroid lesions.

INTRODUCTION
The importance of thyroid cytology in the management of patients with thyroid pathology is highlighted in several guidelines[1]. The workup of any patient requires full and appropriate clinical evaluation (biochemical, immunological, USG, radioisotope and imaging evaluation) before the decision to perform thyroid cytology is undertaken. Thyroid cytology can provide a definite diagnosis of malignancy, with tumor type, enabling appropriate therapeutic surgery in one stage. It can triage the remaining patients into those who potentially require surgical as opposed to medical/endocrinological management. Since the incidence of thyroid malignancy is relatively low and only 1 in 20 clinically identified nodules are malignant[2], thyroid fine needle aspiration can help reduce the rate of surgery for benign thyroid disease. Aspiration cytology of the thyroid is found to be a valuable adjunct to pre-operative screening in the diagnosis of thyroid lesions[3]. Aspiration under ultrasound guidance is now widely used, particularly for nodules deep in the neck and when aspiration fails to yield adequate cellular material and it contributes to diagnostic accuracy[4]. There is an ongoing debate as to appropriate evaluation and management of individuals with thyroid masses. Need to address these issues and to provide a
clinically applicable and cost effective approach to the evaluation and management of thyroid masses has prompted to take up this study.

FNA of thyroid nodules has many advantages:

1. Safe, simple, cost-effective procedure with absence of major complications and can be performed on out-patients with wide patient compliance.

2. Provides a more rapid and accurate diagnosis of the thyroid lesions than any other combination of clinical / laboratory tests[3,5].

Like any other diagnostic test FNA has some inherent limitations. Two issues in thyroid FNA are responsible for the majority of erroneous cytology reports:

1. Inaccuracy and inadequacy of samples

2. Inability to accurately subtype follicular neoplasms

**MATERIALS AND METHODS**

Medical records were reviewed for the patients with thyroid enlargement during the last 2 year period from Jan 2008-Dec 2010 who subsequently underwent thyroid resection at Maharajahs Institute of Medical Sciences, Vizianagaram. The aspiration was done under aseptic conditions with 23 gauge needle fitted to a 5ml syringe. Several smears were prepared and promptly fixed in 95% ethyl alcohol. These were stained with papanicolaou stain and haematoxylin stain. Whenever fluid was obtained, centrifuged smears were made from the sediment and stained by the above stains. The cytology results were categorized into four categories as benign(negative), suspicious (indeterminate for malignancy), malignant and unsatisfactory / non-diagnostic. Aspirates classified as benign included colloid goiter, colloid or adenomatous nodule, hashimotos thyroiditis, sub-acute thyroiditis, thyroglossal duct cyst. Suspicious smears included follicular neoplasms, cellular adenomatoid nodules, hurthle cell proliferations and lesions suspicious for papillary carcinomas. Aspirates with insufficient cellularity or poor quality smear due to delayed or inadequate fixation were considered unsatisfactory.

An adequate sample must be taken and adequate in amount. Criteria proposed for adequacy of thyroid cytology is 5-6 groups of well preserved follicular epithelial cells with ≥10 cell per group, the smear should be technically well prepared, the aspirate should be properly smeared to avoid clotting and lastly smears should be read in clinical context[3]. Aspirations considered unsatisfactory should be repeated because cancer has been reported in 5-15% of these cases[4].

Whenever the excised specimen was received in the department, it was routinely processed to obtain paraffin sections which were stained by H&E stain. Results of cytological and histopathological studies were later correlated to evaluate the efficiency of FNAC. Diagnostic accuracy of FNA was calculated.

Hence thyroid aspiration is useful:

1. To detect patients with thyroid malignancy (sensitivity)

2. To exclude patients without malignancy (specificity)

3. To predict the presence/absence of cancer (positive and negative predictive value)

4. To correctly classify patients as those who should have their thyroid masses excised and those for whom excision is unnecessary (efficiency)

**RESULTS**

In our study the mean age of patients was 38yrs with range of 9 – 60 yrs. Most of the patients were in the age group of 31 – 50 yrs.

Most of the patients were females: 127 (90.71%) out of the total 140 cases.

Male to female ratio was 1:9.77.

Of the total 140 cases of FNAC, 116 cases (82.85%) were non-neoplastic and 22 (15.72%) were neoplastic lesions (as shown below in table I and fig I).

**Table I:** shows total no. of cases

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No of cases</th>
<th>%age of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign lesions</td>
<td>131</td>
<td>93.87</td>
</tr>
<tr>
<td>Malignant lesions</td>
<td>09</td>
<td>06.43</td>
</tr>
<tr>
<td>Total</td>
<td>140</td>
<td>100</td>
</tr>
</tbody>
</table>
Of the benign/non-neoplastic diagnosis, colloid goiter was the most common thyroid lesion diagnosed in 104 cases (74.29%) cases. The other benign lesions diagnosed were Hashimoto's thyroiditis in 5 (3.51%) cases, De Quervain's thyroiditis in 2 (1.43%) cases, thyroglossal duct cyst in 3 (2.14%) cases, and hyperthyroidism in 2 (1.43%) cases (as shown below in Table II and Fig II).

**Figure 3**
Table 2: Incidence of non-neoplastic thyroid lesions according to FNAC

<table>
<thead>
<tr>
<th>S. no</th>
<th>Non-neoplastic cytological diagnosis</th>
<th>No of cases</th>
<th>Percentage of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Simple colloid goiter</td>
<td>49</td>
<td>35.00</td>
</tr>
<tr>
<td>II</td>
<td>Nodular colloid goiter</td>
<td>19</td>
<td>13.37</td>
</tr>
<tr>
<td>III</td>
<td>Colloid goiter with haemorrhage</td>
<td>9</td>
<td>5.43</td>
</tr>
<tr>
<td>IV</td>
<td>Colloid goiter with cystic degeneration</td>
<td>12</td>
<td>2.57</td>
</tr>
<tr>
<td>V</td>
<td>Colloid goiter with adenomatous hyperplasia</td>
<td>15</td>
<td>10.71</td>
</tr>
<tr>
<td>VI</td>
<td>Hashimoto's thyroiditis</td>
<td>5</td>
<td>3.57</td>
</tr>
<tr>
<td>VII</td>
<td>De Quervain's thyroiditis</td>
<td>2</td>
<td>1.43</td>
</tr>
<tr>
<td>VIII</td>
<td>Thyroglossal duct cyst</td>
<td>3</td>
<td>2.14</td>
</tr>
<tr>
<td>IX</td>
<td>Hyperthyroidism</td>
<td>2</td>
<td>1.43</td>
</tr>
</tbody>
</table>

Of the malignant lesions on cytology, follicular neoplasm constituted a total of 13 cases (9.29%) and papillary carcinoma diagnosed in 9 (6.43%) cases (as shown in Table 3).

**Figure 4**

**Figure 5**
Table 3: Incidence of Neoplastic thyroid lesions according to FNAC

<table>
<thead>
<tr>
<th>Neoplastic diagnosis</th>
<th>No of cases</th>
<th>% age of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicular neoplasm</td>
<td>13</td>
<td>9.29</td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>9</td>
<td>6.43</td>
</tr>
</tbody>
</table>

**Figure 6**
Table 4: Cytohistopathological correlation of thyroid lesions

<table>
<thead>
<tr>
<th>Cytological diagnosis</th>
<th>Histopathological diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colloid goiter</td>
<td>35 (Histopathological)</td>
</tr>
<tr>
<td>Hashimoto's thyroiditis</td>
<td>2 (Histopathological)</td>
</tr>
<tr>
<td>Follicular neoplasm</td>
<td>2 (Histopathological)</td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>9 (Histopathological)</td>
</tr>
</tbody>
</table>

Histopathological diagnosis was available (as shown in Table II above) in 52 cases. 6 cases of follicular neoplasms on FNA which were subsequently examined on histopathology were found to be follicular adenoma in 3 cases, colloid goiter in 2 cases and follicular carcinoma in 1 case. 2 cases of Hashimoto's thyroiditis were confirmed histologically. All 9 cases of malignancy reported on FNA as papillary carcinoma were confirmed as malignancy on biopsy.

Hence, after comparison of results of FNAC with histopathology, FNA showed overall diagnostic accuracy of 92.3% with specificity of 90.0%, sensitivity of 100% for malignant lesions, positive predictive value of 100% for malignancy and negative predictive value of 90.5% in our study.

**DISCUSSION**

All types of false negative and false positive results cause concern because the reliability of cytology is in question. However, it is difficult to calculate the true frequency of false negative results because only a small percentage of patients with benign cytological findings undergo surgery. False negative FNA cytology results were found in four of our patients which is less as compared to other studies where the values range from 1-16% [6,7,8]. False negative rate in our study was 3.85%. Apparently false negative cases are encountered when there are no recognizable diagnostic cells in the smear because of sampling or processing error. The incidence of false negative in diagnosis of thyroid aspirates may be high and is usually attributable to overlooking of malignancy in favour of follicular adenoma, cystic lesions
and Hashimoto's thyroiditis.

False positive result cytology are uncommon and were not found in any patient in our study. This finding is consistent with the other reports that cited rate ranging from 0 – 9%. False positive diagnosis is the result of misinterpretation of the nature of benign cell than a sampling error. False positive diagnosis are usually encountered in Hashimoto's thyroiditis, follicular/parathyroid/atypical adenoma, colloid nodule.

The categorization of cytological results into benign, suspicious, malignant and unsatisfactory/inadequate is necessary to allow clinicians to use cytology results to guide the patient management with specific reference to surgery. Follicular neoplasms form a gray zone with differential diagnosis including follicular carcinoma, follicular variant of papillary carcinoma, follicular adenoma and adenomatoid nodule. Follicular adenoma and follicular carcinoma requires detailed histopathological examination for vascular and capsular invasion.

Many papers on the diagnostic sensitivities for thyroid nodules exist in the literature, showing a wide range from 43 – 100% and specificity from 47 – 100%. Factors contributing to this broad range of sensitivity and specificity are the handling of suspicious cases, adequacy of sample, sampling techniques, experience of pathologist in interpretation, length of follow up and inclusion of suspicious/indeterminate cases in the category of false negative diagnosis. In our study, the specificity for cytological diagnosis of neoplasia was 90.0%, sensitivity of 100%, positive predictive value of 100%, negative predictive value of 97.67% and diagnostic accuracy of 92.3%. The results are comparable with the other studies. Afroze et al (2002) reported in his study sensitivity of 61.9%, specificity of 99.3%, negative predictive value 94.7%, positive predictive value 92.8% and accuracy of 94.5%. Ikram et al has reported sensitivity and specificity for malignancy as 100% which is higher than our results as they do not have false positive results in their study due to small number of patients. Kessler et al, 2005, reported 79% sensitivity, 98.5% specificity, negative predictive value 76.6%, positive predictive value 98.7% and diagnostic accuracy of 87%. Gupta et al, 2006, reported 80% sensitivity, 86.6% specificity, 86.6% negative predictive value, positive predictive value of 80% and accuracy of 84%. Mahar SA et al (2006) reported a sensitivity of 98%, specificity of 70% with positive predictive value of 91%, negative predictive value of 93% and diagnostic accuracy of 91%.

CONCLUSION

FNA is the most recommended diagnostic procedure for the diagnosis of thyroid lesions since it allows the distinction between benign and malignant lesions and helps to design the treatment plans. Technical procedure for the aspiration and smear preparation are important steps for obtaining suitable smears. Adequacy of the specimen (must be representative of the lesion), adequate in amount and read in clinical context will reduce false positive numbers. If the cytologic report is malignant, surgery is the recommended procedure; for suspicious lesion, respiration is required; for benign report no further immediate diagnostic studies are required.

Ongoing histocytological correlation is an important quality control assurance measure and allows labs to calculate there false positive and false negative rates. Hence, FNA is an invaluable tool in the management of thyroid lesions with a high degree of accuracy.

References

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20. Cooper's D S , Doherty G M , Haugen B R et al. Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid 2006 ; 16 : 4 – 33
Author Information

Sandhya Panjeta Gulia, MD Pathology
Assistant Professor, Dept of Pathology, Sri Venkateshwaraa Medical College Hospital and Research Centre

Madhusudhan Chaudhury
Professor, Dept of Pathology, Sri Venkateshwaraa Medical College Hospital and Research Centre

Emani Sitaramam, MD Pathology
Associate Professor, Dept of Pathology, Maharajahs Institute of Medical Sciences

Karri Prasada Reddy, MD Pathology
Professor, Dept of Pathology, Maharajahs Institute of Medical Sciences