A Comprehensive Analysis of Thyroid Lesions: Cytomorphological Study and Categorization using the Bethesda System in a Tertiary Care Hospital

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Abstract: Thyroid disorders are among the most common endocrine disorder encountered in routine clinical practice. Evaluating thyroid lesions and reaching a clinical diagnosis can be challenging. FNAC (Fine needle aspiration cytology) of thyroid is commonly used and highly effective tool for diagnosis and managing patients with thyroid nodules. This study, conducted in department of pathology, at Government Medical College, Surat, aims to report on thyroid cytology smears categorized using the Bethesda system of thyroid cytopathology TBSRTC and to correlate these with histopathological findings. FNAC was performed on total 175 cases presented with thyroid swelling and these cases were categorized according to TBSRTC. The cytological diagnosis was than correlated histopathologically. Results: FNAC was carried out in 175 cases, diagnostic categories includes 8% non-diagnostic, 82.26% benign, 2.80% Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance, 0.5% follicular neoplasm or suspicious for follicular neoplasm, 4% suspicious for malignancy and 2.28% malignant lesions. Subsequent histopathological correlation was possible in 44 cases. Conclusion: Standardized categorical Bethesda systems for reporting thyroid FNAC can make results easier to understand and interpret for clinicians and give clear indications for therapeutic action.

Keywords: Bethesda System, Fine Needle Aspiration Cytology, Histopathology

1. Introduction

In clinical practice, thyroid disorders are most commonly encountered endocrine disorders.¹ ² The majority of solitary thyroid nodules are benign; the incidence of malignancy being only 5-20% of surgically excised thyroid nodules on histopathology. Thus, to separate benign nodules (the majority) from malignant lesions is the primary challenge in management of solitary thyroid nodule. Fine Needle Aspiration Cytology (FNAC) is first-line, simple, cost effective, minimally invasive and quick screening test as well as the diagnostic tool.²³ FNAC helps in triaging the patients who require surgery for a neoplastic disorder from those who have a functional or inflammatory abnormality and who can be followed clinically or treated medically.³ Despite its widespread use, it suffered from a reporting confusion due to various reporting formats of thyroid FNA varying from two category to six or more category schemes. While some of them tried to diagnose various lesions using histology-equivalent categories, other formats had categories like equivocal, inconclusive, indeterminate, atypical, suspicious, uncertain, malignancy suspicious, possibly neoplastic, possibly malignant and probably malignant to report thyroid aspirates that fell between benign and malignant diagnostic categories.²³ These made it difficult for clinicians to interpret the reports. To address terminology and other issues related to thyroid FNA, the National Cancer Institute (NCI) hosted the “NCI Thyroid FNA State of the Science Conference,” and proposed the Bethesda System for Reporting Thyroid Cytopathology. This was a standardized system with six general diagnostic categories and clear categorical nomenclature including ([TBSRTC]) which includes definitions, diagnostic/morphologic criteria, explanatory notes, malignancy risks and a brief management plan for each diagnostic category.⁶

TBSRTC provides a 6-tiered diagnostic framework that uses defined criteria to promote uniformity in the reporting of thyroid aspirates. One of the major advantages of this scheme is that the individual diagnostic categories are associated with defined risks of malignancy, allowing for standardized management algorithms for each diagnosis.

The objective of this retrospective study, done to report thyroid cytology smears by TBSRTC into various diagnostic categories, analyze their cytological features using TBSRTC monograph, conveying brief management plan to the clinicians, and correlate with histology of surgical specimens received.

2. Material and Method

This retrospective study was conducted in the Department of Pathology, Government Medical college, Surat from January 2019 to December 2019. All the patients with clinically diagnosed Thyroid lesions referred for Thyroid FNAC were included in the study. Neck swellings other than thyroid swellings and patients having known Bleeding diathesis were excluded. FNAC was performed after taking informed consent from the patient.

Our study was undertaken to evaluate cytomorphology in outdoor and indoor patients presenting with palpable thyroid lesions and compared them histopathologically. Wherever

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specimen was received after surgery to determine its diagnostic accuracy. After careful examination and palpation, FNA was done under aseptic precautions and material was deposited on several clean and labelled glass slides and stained by routine H and E, Pap, MGG stain. All the slides were examined thoroughly and reporting was done according to The Bethesda System for Reporting Thyroid Cytology (TBSRTC).

During the period of this study from January 2019 to December 2019, total 175 FNA was done from thyroid, among them 18 specimens of thyroid were received after surgery and subjected to histopathological study. All the specimens were fixed in 10% formalin. Detailed gross examination was done and sections were given from selected representative area for routine paraffin processing. Slides were stained by H and E stain. Correlation of cytological and histopathological findings was performed whenever possible.

3. Results

FNAC was performed on total 175 patients who were presented with thyroid nodule or swelling. Age of the patients ranged from 7-83 years. Most of the patients presented in age group of 21 to 30 years. In our study 29 (16.57%) cases were of males and 146 (84%) cases were of females. Male to female ratio was 1:5.2

The distribution of 175 cases is shown in Table 1. Benign category was the largest (84.5%) with 144 cases, followed by ND/UNS category (7%) with 14 cases. Malignant and SFM categories constituted 4% with 5 cases and 2.28% with 4 cases respectively, making a total of 6.28%. A US/FLUS constituted (2.8%) with 5 cases, while FN/SFN had 0.5% with one case only.

<table>
<thead>
<tr>
<th>BethesdaDiagnostic categories</th>
<th>No of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category I - Nondiagnostic or Unsatisfactory</td>
<td>14</td>
<td>8%</td>
</tr>
<tr>
<td>Category II - Benign Thyroid Lesion</td>
<td>144</td>
<td>82.28%</td>
</tr>
<tr>
<td>Category III - Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance</td>
<td>5</td>
<td>2.8%</td>
</tr>
<tr>
<td>Category IV - Follicular Neoplasm or Suspicious for a Follicular Neoplasm, specify if Hurthle cell (oncocytic) type</td>
<td>1</td>
<td>0.5%</td>
</tr>
<tr>
<td>Category V - Suspicious for Malignancy</td>
<td>7</td>
<td>4%</td>
</tr>
<tr>
<td>Total</td>
<td>175</td>
<td>100.00%</td>
</tr>
</tbody>
</table>

The study showed 14 cases in ND/UNS category. These cases were categorized as non-diagnostic when the adequacy criteria laid down by the Bethesda system was not fulfilled. In our study, 14 smears were unsatisfactory owing to presence of only cystic fluid (5 cases), obscuring blood, overly thick smears or an inadequate number of follicular cells.

Category II – Benign included 144/175 cases (82.28%). Majority of the cases in Category II were Benign Follicular Nodule (Colloid nodule/Adenomatoid nodule) accounting for 115 cases (79.86%), followed by Hashimoto/Lymphocytic thyroiditis with 29 (20.13%). Histopathological details were available in 34 cases of Benign Follicular Nodule, which showed positive correlation.
In present Study in TBS category-III (Atypia of Undetermined Significance/ Atypical Follicular Lesion of Undetermined Significance, included total 5/175 cases.

Category IV- Follicular Neoplasm (FN) or Suspicious for a Follicular Neoplasm (SFN) included 1/175 cases (17.14%) of which histopathological examination showed follicular carcinoma.

Category V- Suspicious for Malignancy (SFM) included 7 cases (1.14%) which was diagnosed as suspicious of papillary thyroid carcinoma on cytology. Resected Surgical specimen was received in all 5 cases and histopathological findings favors diagnosis of papillary carcinoma.

Category VI- Malignant included 4 cases (2.86 %). Out of which, 1 cases was diagnosed as Papillary carcinoma .1 as medullary carcinoma and the remaining 2 as Anaplastic carcinoma on cytology smear. Resected Surgical specimen were received in 2 cases, the cytological and histopathological findings of which correlated with a diagnosis of Papillary carcinoma and anaplastic carcinoma.

<table>
<thead>
<tr>
<th>Category</th>
<th>No of cases in this category</th>
<th>No of cases available for HPE</th>
<th>FNA diagnosis</th>
<th>HP diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>14</td>
<td>-</td>
<td>-</td>
<td></td>
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<tr>
<td>II</td>
<td>146</td>
<td>34</td>
<td>BFN</td>
<td>2 hasimotos</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>30 colloid Goiter</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 MNG</td>
</tr>
<tr>
<td>III</td>
<td>5</td>
<td>2</td>
<td>AUS</td>
<td>Folicular adenoma</td>
</tr>
<tr>
<td>IV</td>
<td>1</td>
<td>1</td>
<td>SFN</td>
<td>1 Follicular carcinoma</td>
</tr>
<tr>
<td>V</td>
<td>7</td>
<td>5</td>
<td>PTC</td>
<td>1 NIFTP</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 FVPTC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3 PTC</td>
</tr>
<tr>
<td>VI</td>
<td>4</td>
<td>2</td>
<td>Undifferentiated Medullary</td>
<td>Anaplastic carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Medullary carcinoma</td>
<td></td>
</tr>
</tbody>
</table>

4. Images

Figure 1: Lymphocytic Thyroiditis (Giemsa stain 40x), CAT II

Figure 2: Microfollicular pattern of thyroid cells (Giemsa stain 40x), CAT II

Figure 3: Papillary thyroid carcinoma (H&E stain 10x) CAT V

Figure 4: Suspicious of Medullary thyroid carcinoma (H&E stain 10x) CAT IV

5. Discussion

FNA plays an evolutionary role in the interpretation and evaluation of thyroid lesions. In international guidelines,
high resolution ultrasonography and FNA biopsy are recommended as the first line evaluation tools of thyroid nodules. Although thyroid ultrasonography is convenient and noninvasive, the ultrasound features are not adequately sensitive to detect all thyroid lesions. Hence, thyroid FNA is the most important diagnostic tool for thyroid lesions.

TBSRTC consists of six diagnostic categories, each associated with an implied ROM that translates directly into a clinical management algorithm. TBSRTC not only included the diagnostic designations for the commonly encountered benign and malignant thyroid lesion but also for those who are often diagnosed as “indeterminate for malignancy” (the so called ‘gray zone’) and was sub classified into the three diagnostic categories such as (i) atypia of undetermined significance/follicular lesion of undetermined significance; (ii) follicular neoplasm (FN)/suspicious for a FN; and (iii) suspicious for malignancy. The second edition of TBSRTC has covered potential impact of noninvasive follicular neoplasm of thyroid with papillary like nuclear features (NIFTP) on the indeterminate diagnostic categories. The clinical importance of thyroid nodules lies in the fact that although most nodules are benign, they may be the first sign of malignancy. For clarification and communication to clinicians, the FNAC report format should contain either one of the six tiered Bethesda category. Each category has an implied cancer risk ranges from 0% to 3% for the benign category to virtually 100% for the malignant category which we found in our study.

In present study, one case of atypia of undetermined significance (TBSRTC category III) was diagnosed as adenomatoid goiter with degenerative changes on histopathology. This was due to degenerative changes in adenomatoid goiter with large nuclei having prominent nucleoli and degenerative changes in cytology smears. On histopathology it was correctly diagnosed as adenomatoid goiter with degenerative changes.

6. Conclusion

We found nearly validated accuracy of FNAC by adopting TBSRTC. Therefore, we recommend to implement TBSRTC routinely in our center with ultrasound screening as the initial workup of patients with thyroid swellings. Surgical follow up in every indeterminate indexed cases (Bethesda Categories III and IV) is mandatory to appropriately assess the ROM.

TBSRTC monograph is briefly written in an easy-to-read format and has color photographs which help in cytological diagnosis. Standardized diagnostic systems for Thyroid FNAC reporting can make results easier to understand for clinicians and give clue for therapeutic action. However, The skill of person doing aspiration, location of target lesion, careful reporting FNAC is the key to true diagnosis and proper treatment in thyroid mass. In the modern era ancillary testing with Immunohistochemistry on the cell block preparation can also help cytologist to arrive correct cytological diagnosis.

Table 3: Comparative study of thyroid lesions according to TBSRTC

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<tr>
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<tbody>
<tr>
<td>I</td>
<td>6.6</td>
<td>4.57</td>
<td>5.2</td>
<td>7.2</td>
<td>0.025</td>
<td>2.09</td>
<td>5.2</td>
<td>8%</td>
</tr>
<tr>
<td>II</td>
<td>82</td>
<td>68.57</td>
<td>89.9</td>
<td>80</td>
<td>82.5</td>
<td>89.67</td>
<td>87.60</td>
<td>82.28%</td>
</tr>
<tr>
<td>III</td>
<td>2</td>
<td>5.7</td>
<td>0</td>
<td>4.9</td>
<td>0.02</td>
<td>5.97</td>
<td>2.80</td>
<td>2.8%</td>
</tr>
<tr>
<td>IV</td>
<td>2.5</td>
<td>17</td>
<td>2.3</td>
<td>2.2</td>
<td>2</td>
<td>1.45</td>
<td>2.40</td>
<td>0.5%</td>
</tr>
<tr>
<td>V</td>
<td>1.6</td>
<td>1.14</td>
<td>0.3</td>
<td>3.6</td>
<td>0.01</td>
<td>0.29</td>
<td>1.60</td>
<td>4%</td>
</tr>
<tr>
<td>VI</td>
<td>5.1</td>
<td>2.86</td>
<td>2.3</td>
<td>2.2</td>
<td>6</td>
<td>0.58</td>
<td>0.40</td>
<td>2.28%</td>
</tr>
</tbody>
</table>

In the present study, no complication like hematoma, laryngeal nerve palsy or perforation of trachea was noted. Evaluation of FNA smears was done according to the Bethesda system for reporting thyroid cytopathology. Out of 175 cases, histopathological correlation was done in 44 cases. The study showed M:F ratio 1:5.03 which was comparable with study of Rajesh et al\(^1\), Amit et al\(^2\) and Sharma et al\(^10\) showed M:F ratio 1:7.6, 1:7.6 and 1:5.2 respectively. Present study showed maximum no of cases in 21-30 yrs age group with 33.48% which was compatible with study done by Nikita et al\(^12\), Rajesh et al and Amit garit with 31.20%, 29.14%, 26.22% and 24% respectively.

Factors responsible for nondiagnostic FNAC results which including personal skill, the nature of the thyroid nodules, vascularity of thyroid lesion, criteria used to judge adequacy of the smears, and the cystic area of the nodule. According to TBSRTC category III should not exceed more than 7%. In our study, there were 7(2.8%) cases of category III, which was within defined limit.

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