THE BETHESDA SYSTEM FOR REPORTING THYROID CYTOPATHOLOGY: A TWO YEAR INSTITUTIONAL AUDIT

Salma Bhat¹, Nazia Bhat¹, Humaira Bashir¹, Summiya Farooq¹, Ruby Reshi¹, Mir Junaid Nazeir², Isma Niyaz¹

¹Department of Pathology, Government Medical College, Srinagar; ²Department of Radiodiagnosis, Government Medical College, Srinagar.

ABSTRACT

Fine needle aspiration cytology (FNAC) of thyroid plays a significant crucial role in cytopathology worldwide. Thyroid FNAC is extremely useful in identifying a substantial proportion of thyroid nodules as benign and reducing unnecessary surgery for patients with benign disease. The present study was done with the aim of stratifying thyroid cytology smears by The Bethesda System For Reporting Thyroid Cytopathology (TBSRTC) into various diagnostic categories, analyze their cytological features using TBSRTC monograph, convey brief management plan to the clinicians, and correlate with histology of surgical specimens received.

Methods: This was a prospective study done on 600 cases of fine needle aspirations of thyroid nodules over a period of two years from July 2013 to June 2015.

Results: Mean age of the patients included in the study was 36 years (11–73) and male to female ratio was 2:6. Out of total 600 cases, 40 cases were non diagnostic (Bethesda Category I), 492 cases were diagnosed as benign (Bethesda category II) and 12 were Bethesda category III while 41 cases were categorized as either malignant or suspicious for malignancy (Bethesda category V and VI). Histopathologic correlation was available in 113 cases.

Conclusion: TBSRTC is an excellent reporting system for thyroid cytopathology. It also provides clear management guidelines to clinicians to go for follow up FNA or surgery and also the extent of surgery.

Key Words: Thyroid nodule, Cytology, The Bethesda system, Histopathology

INTRODUCTION

Fine needle aspiration cytology (FNAC) of thyroid plays a significant crucial role in cytopathology worldwide. Thyroid FNAC is very useful in identifying a substantial proportion of thyroid nodules as benign and reducing unnecessary surgery for patients with benign disease.¹ To address terminology and other issues related to thyroid FNACs, The National Cancer Institute (NCI) sponsored the NCI Thyroid Fine-needle Aspiration (FNA) State of the Science Conference on October 22-23, 2007 in Bethesda, MD. The meeting concluded with the introduction of “Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)” which summarizes matters regarding diagnostic terminology/classification scheme for thyroid FNA interpretation and cytomorphic criteria for the diagnosis of various benign and malignant thyroid lesions.² The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) has attempted to standardize reporting and cytological criteria in aspiration smears.³ TBSRTC is a six-category scheme of thyroid cytopathology reporting. Each category has an implied cancer risk, which ranges from 0% to 3% for the “benign” category to virtually 100% for the “malignant” category.⁴

The present study was done with the aim of stratifying thyroid cytology smears by TBSRTC into various diagnostic categories, analyze their cytological features using TBSRTC monograph, convey brief management plan to the clinicians, and correlate with histology of surgical specimens received.

MATERIALS AND METHODS

This was a prospective study done over a period of two years from July 2013 to June 2015. A total of 600 fine needle aspirations (FNA) of thyroid nodules were performed during...
this time period. Smears were stained with MGG and PAP stain. All fine needle aspiration cytology (FNAC) diagnoses were classified according to TBSRTC into NonDiagnostic/Unsatisfactory (ND/UNS), Benign, Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance (AUS/FLUS), Follicular Neoplasm/Suspicious of a Follicular Neoplasm (FN/SFN), Suspicious for Malignancy (SFM), and Malignant. Histopathological correlation was done, where ever surgical material was available.

RESULTS

Mean age of the patients included in the study was 36 years (11–73) and male to female ratio was 2:6. Out of total 600 cases, 40 cases were non diagnostic (Bethesda Category I), 492 cases were diagnosed as benign (Bethesda category II) and 12 were Bethesda category III while 41 cases were categorized as either malignant or suspicious for malignancy (Bethesda category V and VI) as shown in Table 1. Histopathologic correlation was done in 113 cases which further underwent surgical intervention. For Bethesda V and VI category, 100% concordance was found, however for Bethesda category II, 5 out of 70 cases were found to have malignant diagnosis on final histopathology. The distribution of various categories from 600 evaluated thyroid nodules are shown in table 1.

The present study had 40 (6.6%) 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, 40 smears were unsatisfactory owing to presence of only cystic fluid, obscuring blood, overly thick smears or an inadequate number of follicular cells.

76.4% of all cases in the benign category were consistent with benign colloid/adenomatous colloid nodule. Smears showed macrofolicular fragments with Hurthle cell features against a colloid background. Rare microfolicles were present. No significant pleomorphism or nuclear atypia was seen. High cellularity was not seen. Hurthle cells were present only in 4.7% cases and macrophages were present in 31.7% cases.

Chronic lymphocytic thyroiditis constituted 17.6% of cases in the benign category. Aspirates of chronic lymphocytic thyroiditis were characterized by a population of lymphocytes, plasma cells, and lymphohistiocytic aggregates, and occasional cohesive clusters of follicular cells with oncocytic features (Hurthle cells). Lymphohistiocytic aggregates with associated follicular dendritic cells and tingible body macrophages are often easily identified (Fig 1).

Aspirates of subacute thyroiditis were mostly hypocellular and consisted of multinucleated giant cells and loose aggregates of epithelioid histiocytes (granulomas). A variable amount of background mixed inflammatory cells including lymphocytes, plasma cells, eosinophils, and neutrophils was seen in 40% cases of subacute thyroiditis.

In this study, category AUS/FLUS constituted 2% of all the cases. 65% of these were moderately cellular smears with occasional microfolicular pattern (Fig 2), 20% showed sparsely cellular smear with prominent microfolicles and scant colloid and 15% showed predominantly benign appearing smear with focal features of papillary thyroid carcinoma (PTC) including nuclear grooves, crowding, pale chromatin and alterations in nuclear contour and shape.

There were 15 cases (2.5%) in the category of Follicular neoplasm/Suspicious of Follicular neoplasm. Smears were highly cellular with predominant microfolicle formations and scant colloid (Fig 3). Lesions exhibiting Hurthle cell change predominantly and diagnosed as Suspicious for Hurthle cell neoplasm were also included.

In cases of suspicious papillary carcinoma included in TBSRTC category V presence of nuclear enlargement, grooves, crowding along with thick colloid were considered mainly cellular with crowded cell groups exhibiting nuclear and cytoplasmic pleomorphism with some occasional single atypical cells (Fig 4).

Lesions were classified into Bethesda category VI category if they were diagnosed as frankly malignant with type specific. There were 10 and 31 cases in Bethesda category V and VI respectively in our study.

DISCUSSION

This study shows the two-year experience in reporting thyroid aspirations by TBSRTC in a Medical college hospital. The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) improves the clarity of communication between cytopathologists and clinicians, predicts the cancer risk and reduces unnecessary surgery for patients with benign nodules and appropriately triages patients with malignant nodules for timely surgical intervention. TBSRTC does not recommend surgery for ND/UNS, benign and AUS/FLUS category. In the FN/SFN, SFM, and malignant categories, excision of nodules or partial/complete thyroidectomy was performed as per TBSRTC recommendations.

TBSRTC Category I—nondiagnostic or unsatisfactory (ND/UNS)

A thyroid FNA sample is considered adequate for evaluation if it contains a minimum of six groups of well-visualized follicular cells, with at least ten cells per group preferably on a single slide. The use of these well established criteria
for adequacy is helpful because they improve the diagnostic efficiency of thyroid FNA and avoid unnecessary surgery for benign non-neoplastic thyroid lesions. Ten patients came back for a repeat FNAC after a 3 month period out of which one case after a repeat FNAC revealed features suspicious for PTC which was confirmed on histopathology. Renshaw found that patients with at least two non-diagnostic FNAC had significantly lower risk of malignancy (0%) compared to those who had only one non-diagnostic FNAC (20%).

**TBSRTC Category II—benign**

The benign category had 492 cases (82%) with BFN being the predominant group followed by Lymphocytic thyroiditis and Granulomatous thyroiditis. The benign category comprised 80% of all cases stratified according to TBSRTC in a study by Mehra P et al. Surgical follow up was available in 35 cases diagnosed as BFN on cytology. 24 cases were reported as colloid goitre, 8 as Follicular adenoma and 3 as PTC on histopathology. Cases of PTC were incidental findings in thyroid specimen and were mural nodules in a cystic lesion. There were no lymph nodes in these cases and ultrasound features were not suspicious. Ultrasound guided FNAC that can obtain material from the wall and solid part of the cyst increases the accuracy of FNAC in cystic PTC. The recommended management of this category is clinical follow up.

**TBSRTC Category III—atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS)**

Cases considered as AUS/FLUS are those for which cytological findings are not convincingly benign, but the degree of architectural and cellular atypia is also not sufficient for a diagnosis of follicular neoplasm or suspicious for malignancy. In our series, the FLUS category represented 2% of all thyroid FNAs over a 2-year period.

Recent series that reported experiences with the TBSRTC categories showed that the AUS/FLUS category exhibited a marked variability in incidence (0.7-18%) and malignant outcome (6-48%) in resection specimens. The recommended management protocol is repeat FNA after sufficient time gap. We advised the same in all our 12 cases.

**TBSRTC Category IV—FN or suspicious for a FN (FN/SFN)**

Aspirates with cytomorphic features of moderate to high cellularity, scant or absent colloid, with predominantly microfollicular arrangement of follicular cells in repetitive pattern were grouped under the Follicular neoplasm/suspicious for a follicular neoplasm (FN/SFN) category. Aspirates with cytomorphic characteristics of Hurthle cell neoplasm were also placed in this category.

About 15–30% of these cases called FN/SFN prove to be malignant [12,13] the rest being FAs or cellular adenomatous nodules of MNG. TBSRTC recommends lobectomy for this category. Six specimens were received 1 of which turned out to be follicular variant of papillary carcinoma, 1 of follicular carcinoma (Fig 5) and the other 4 were follicular adenomas.

**TBSRTC Category V—suspicious for malignancy**

Many thyroid malignancies like papillary thyroid carcinoma can be diagnosed with certainty by FNA. But the nuclear and architectural changes of some PTCs are subtle and focal. This is especially true for the follicular variant of PTC, which can be difficult to distinguish from a benign follicular nodule. If only one or two characteristic features of PTC are present and are only focal, or the sample is sparsely cellular a malignant diagnosis cannot be made with certainty. Such cases are best classified as suspicious for malignancy. Most (60–75%) of these cases prove to be papillary thyroid carcinomas and the rest are mostly adenomas. The same general principle applies to other thyroid malignancies like medullary carcinoma and lymphoma, where ancillary tests help.

Ancillary tests may be useful for patients with a diagnosis of suspicious for medullary carcinoma. An elevated serum calcitonin and/or a repeat FNA that shows strong immunoreactivity for chromogranin, synaptophysin and calcitonin can convert a category V diagnosis of medullary carcinoma to a category VI or definite diagnosis of malignancy. TBSRTC recommends near-total thyroidectomy or surgical lobectomy for cases in this category.

**TBSRTC Category VI—malignant**

This TBSRTC category is applied whenever the cytomorphic features are conclusive for malignancy. The criteria for reporting PTC are follicular cells arranged in papillary or syncytial like monolayers, cells with squamous metaplasia, altered follicular cells exhibiting characteristic nuclear features like enlarged oval or irregular molded nuclei, longitudinal nuclear grooves, intranuclear cytoplasmic pseudo inclusions, pale nuclei with powdery chromat and psammoma bodies. In the present study we reported 21 cases of papillary thyroid carcinomas all of which correlated with histology (Fig 6 a&b). The criteria for reporting medullary carcinoma are cellular smears with plasmacytoid, polygonal or spindle shaped cells. Amyloid is often present and appears as dense amorphous material. In this study we diagnosed 6 cases of MTC. Histopathology was available in 4 which correlated with the cytological diagnosis (Fig 7 a&b).

Anaplastic carcinoma is a highly aggressive malignancy of the thyroid that has lost evidence of follicular cell origin. It
accounts for less than 2% of thyroid malignancies, although rates vary geographically, and characteristically it occurs in older adults. The criteria for reporting anaplastic thyroid carcinoma are neoplastic cells arranged in groups or individually with cells having epithelioid, spindled, plasmacytoid or rhabdoid shape. Nuclear pleomorphism, multinucleation and neutrophilic infiltration of tumor cell cytoplasm are other features. Mitotic activity will be numerous and abnormal (Fig 8). In our study we reported 2 cases one of which was confirmed on histopathology. Primary thyroid lymphomas are extremely uncommon neoplasms accounting for 5% of all thyroid malignancies. The criteria for reporting a lymphoma were cellular smears composed of dispersed monotonous lymphoid cells with vesicular chromatin and prominent nucleoli. One primary lymphoma of thyroid was diagnosed on FNAC. The patient received chemotherapy and responded well to the therapy. TBSRTC recommends near-total thyroidectomy for these cases of malignancy.

CONCLUSION

Our study is a prospective analysis of reporting thyroid FNA using the Bethesda system. TBSRTC is an excellent reporting system for thyroid cytopathology. Our study as well as previous various studies highlight the utility of FNAC in thyroid lesions as safe, cost effective, OPD procedure with minimal complications. It further obviates unwanted surgical intervention for benign lesions and provides clear management guidelines to clinicians to go for follow up FNA or surgery and also the extent of surgery.

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REFERENCES

Table 1: Number of cases in various diagnostic categories and subcategories according to the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC).

<table>
<thead>
<tr>
<th>Bethesda Cytological categories</th>
<th>Subcategories</th>
<th>Number of cases</th>
<th>Total number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiagnostic/unsatisfactory (ND/UNS)</td>
<td>Cyst fluid only</td>
<td>23</td>
<td>40(6.6%)</td>
</tr>
<tr>
<td></td>
<td>acellular specimen</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td></td>
<td>clotting artifact, etc.</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Benign</td>
<td>376</td>
<td>492(82%)</td>
</tr>
<tr>
<td></td>
<td>Aadenomatoid nodule, colloid nodule, etc.</td>
<td>87</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lymphocytic(Hashimoto) thyroiditis</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Granulomatous thyroiditis and Others</td>
<td>12(2%)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Atypia of undetermined significance /follicular lesion of undetermined significance(AUS/FLUS)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Follicular neoplasm / suspicious for a follicular neoplasm (FN/SFN)</td>
<td>15(2.5%)</td>
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<tr>
<td>V</td>
<td>Suspicious for malignancy (SFM)</td>
<td>Suspicious for papillary carcinoma</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Suspicious for medullary carcinoma</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Suspicious for metastatic carcinoma</td>
<td>1</td>
<td>10(1.6%)</td>
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<td></td>
<td>Suspicious for lymphoma</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>VI</td>
<td>Malignant</td>
<td>Papillary thyroid carcinoma</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Medullary thyroid carcinoma</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Undifferentiated (anaplastic) carcinoma</td>
<td>2</td>
<td>31(5.1%)</td>
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<td></td>
<td>Squamous cell carcinoma</td>
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<tr>
<td></td>
<td>Undifferentiated Medullary carcinoma</td>
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<tr>
<td></td>
<td>Non-Hodgkin lymphoma</td>
<td>0</td>
<td></td>
</tr>
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Figure 1: Hashimoto’s Thyroiditis. Photomicrograph showing a Hurthle cell group against a polymorphic lymphoid background.

Figure 2: Atypia of undetermined significance. Photomicrograph showing moderately cellular smears with microfollicular pattern.
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Figure 3: Follicular Neoplasm. Photomicrograph showing highly cellular smears comprising of follicular cells having a repetitive microfollicular pattern.

Figure 4: Suspicious of Papillary Thyroid Carcinoma. Photomicrograph showing crowded cell group with nuclear enlargement and cystic macrophages in background.

Figure 5: Follicular Carcinoma. Photomicrograph showing capsular invasion as mushroom shaped tumour bud progressing the fibrous capsule.

Figure 6a: Papillary Thyroid Carcinoma. Photomicrograph showing large pale oval nuclei with prominent intranuclear cytoplasmic inclusion.

Figure 6b: Papillary Thyroid Carcinoma. Photomicrograph showing papillary architecture with characteristic nuclear features and psammoma bodies.

Figure 7a: Medullary Thyroid Carcinoma. Photomicrograph showing cellular smears with poorly cohesive plasmacytoid cells having moderate anisokaryosis, stippled chromatin and binucleation.
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**Figure 7b:** Medullary Thyroid Carcinoma. Photomicrograph showing solid sheets of tumour cells separated by delicate fibrovascular septae.

**Figure 8:** Anaplastic Thyroid Carcinoma. Photomicrograph showing bizarre malignant cells with abnormal mitosis against an inflammatory background.