Original Research Article

Reporting Thyroid Cytopathology Using the Bethesda System: A Major Step Towards Standardization

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Abstract

Background: Fine needle aspiration cytology (FNAC) is a unique first line of investigation for triaging patients with thyroid nodules. It is a simple economical and minimally invasive procedure reducing the rate of unnecessary surgery for patients with benign nodules. *Objective:* The aim of this prospective study was to assess the efficacy of The Bethesda System for Reporting Thyroid Cytology (TBSRTC) in accurate prediction of thyroid lesions on fine needle aspiration (FNA). *Study design:* In this prospective study of 110 FNAC of thyroid nodules referred to the Department of Pathology at Sri Siddhartha Medical College, Tumkur and histopathological report was correlated wherever it was available. *Results:* Of the 110 cases, 0.9% was nondiagnostic, 83.6% were benign, 0.9% were atypical follicular lesion of undetermined significance (AFLUS), 3.6% were suspicious for follicular neoplasm (SFN), 3.6% were suspicious for malignancy, 7.2% were malignant. *Conclusion:* The Bethesda system of Reporting Thyroid Cytopathology (TBSRTC) undoubtedly represents a major step towards standardization, reproducibility and ultimately improves clinical significance, usefulness and predictive value of thyroid FNAC.

Keywords: Thyroid nodule; Fine needle aspiration cytology; The Bethesda system of reporting thyroid cytopathology.
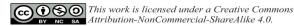
Introduction

Fine-needle aspiration (FNA) has an essential role in the evaluation of euthyroid patients with a thyroid nodule.[1] Before the routine use of thyroid FNA, the percentage of surgically resected thyroid nodules that were malignant was 14%.[1] With current thyroid FNA practice, the percentage of resected nodules that are malignant surpasses 50%.[2] The terminology for thyroid FNA has varied significantly from one laboratory to another, creating confusion in some cases and hindering the sharing of clinically meaningful data among multiple institutions.[1,3] Therefore, consistent diagnostic terminology is imperative, to prevent complications by the historic lack of universal terminology.[4,5] Multiple organizations have proposed diagnostic guidelines for reporting thyroid FNA cytology results, including the Papanicolaou Society of Cytopathology Task Force and the American

Thyroid Association although none have been universally accepted.[6,7] The Bethesda system of interpretation of thyroid FNAC minimises inter observer variations and undoubtedly represents a major step towards standardization, reproducibility and ultimately improved clinical significance, usefulness and predictive value of thyroid FNA.[8](5) The categories under TBSRTC and recommended clinical management are as shown in Table 1.[9,10] The aim of this prospective study was to assess the efficacy of TBSRTC in accurate prediction of thyroid lesions on FNA.

Materials and Methods

This was a prospective study of 110 FNAC of thyroid nodules referred to the Department of Pathology. Complete clinical history was taken, thyroid hormonal profile and imaging studies such as ultrasound were done where necessary. FNAC was done using 23 gauge needles, with or without an airtight syringe, using imaging guidance where ever necessary. The smears were fixed with alcohol and stained with haematoxylin and eosin, and Papanicolaou stain. Thesmears were interpreted by cytopathologist and diagnosis was classified according to TBSRTC (The Bethesda System of Reporting Thyroid Cytopathology), as shown in Table 1. The cytohistological correlation was done where specimen was available. Sensitivity, specificity, positive predictive value and negative predictive value were calculated using histopathological diagnosis as gold standard. The cases were distributed according to the recommended diagnostic categories of the Bethesda System as shown in Table 1.
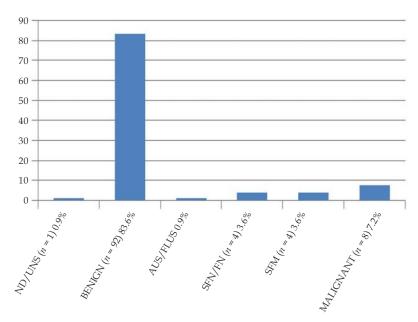
Table 1: TBSRTC: Implied risk of malignancy and recommended clinical management

Diagnostic category	Risk of malignancy (%)	Usual management
Category I: Nondiagnostic or unsatisfactory (ND) Cyst fluid only Virtually acellular specimen Other (obscuring blood, clotting artefact)	1–4	Repeat FNA with ultrasound guidance
Category II: Benign Consistent with benign follicular nodule ((includes adenomatoid nodule, colloid nodule) Consistent with lymphocytic (Hashimoto) thyroiditis in proper clinical context Consistent with granulomatous (subacute) thyroiditis Other	0–3	Clinical follow-up
Category III: Atypia of undetermined significance or follicular lesion of undetermined significance (AUS)	5–15	Repeat FNA
Category IV: Follicular neoplasm or suspicious for follicular neoplasm (SFN) Specify if Hurthle cell (oncocytic type)	15–30	Surgical lobectomy
Category V: Suspicious for malignancy (SFM) Suspicious for papillary carcinoma Suspicious for medullary carcinoma Suspicious for metastatic carcinoma Suspicious for lymphoma Other	60–75	Near-total thyroidectomy or surgical lobectomy
Category VI: Malignant Papillary thyroid carcinoma Poorly differentiated carcinoma Medullary thyroid carcinoma Undifferentiated (anaplastic) carcinoma Squamous cell carcinoma Carcinoma with mixed features (specify) Metastatic carcinoma Non-Hodgkin lymphoma Other	97–99	Near-total thyroidectomy

Results

Age at presentation varied from 16 to 75 year. With a median age being 39 year. Male to female ratio being 1:5.1. The distribution of cases is as shown in Graph 1. In the non-diagnostic category we had one case for which only cyst fluid was aspirated. The commonest cytological diagnostic category was benign (*n* = 92), which had benign follicular nodule (*n* = 59) followed by lymphocytic thyroiditis (*n* = 31). In the category of atypia of undetermined significance there was one case (0.9%) and 4 cases in suspicious for follicular neoplasm (3.9%).

Graph 1: Number of cases in diagnostic categories (*n* = 110)

In the category of suspicious of malignancy there were 04 cases and all the cases were suspicious for papillary carcinoma thyroid.

In the category of malignant there were 8 cases, in which papillary carcinoma was 05 cases (62.5%). Medullary carcinoma was 02 (28.6%), and anaplastic carcinoma was 01 (12.5%).

The sensitivity and specificity of our study were 88.8% and 100% respectively. The positive predictive value and negative predictive value were 100% and 87.5% respectively. If we considered cases of SFM as benign the sensitivity and specificity are as shown in Table 2. If the cases under category of SFM considered as malignant, the values are as shown in Table 3.

Table 2: Cases of SFM as benign the sensitivity and specificity

Category			%
True positive	08	Sensitivity	72.7
False Positive	0	Specificity	100
True Negative	09	Positive predictive value	100
False Negative	03	Negative predictive value	75

Table 3: Cases under category of SFM considered as malignant

Category			%
True positive	10	Sensitivity	100
False Positive	02	Specificity	100
True Negative	08	Positive predictive value	100
False Negative	00	Negative predictive value	70

Discussion

An FNA sample of a thyroid nodule is representative of the underlying lesion, in order to provide useful diagnostic information. For clarity of communication and uniformity of terminology each case has to be reported according to the Bethesda system as each category has an implied cancer risk (ranging from 0 to 3% for the benign category to nearly 100% for malignant category) with rational clinical management guidelines as shown in Table 1.[11, 12]

TBSRTC recommends six categories and suggests that each report should begin with a general diagnostic category. In our study under the nondiagnostic or unsatisfactory (ND/UNS) category there was one case (0.9%) of cyst fluid only, and was advised for repeat aspiration after a minimum period of 3 month, according to the guidelines in TBSRTC, to prevent any false positive interpretation.[1,11] The studies done by Nayar R et al., Theoharis C.G.A, and Ko HM had cases ranging from 1.2% to 16.3% cases in this category.[13–16]

The category of benign had maximum cases, and were distributed as benign follicular nodule (*n* = 59), followed by lymphocytic thyroiditis (*n* = 31). Under the benign category (53.6%), 6 resected specimens were obtained for histopathological examination, of which one case of Hashimoto thyroiditis on cytology showed features of the same on histopathology along with foci of papillary carcinoma. In this case the size of the nodule was less than 1 cm and there were no suspicious findings on ultrasound. Other cases remained concordant with the cytological diagnosis. The studies done by Nayar R, Theoharis C.G.A had values ranging from 34% to 87.5% in this category.[15,16]

The category of atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS), has been a source of confusion for both clinician and Pathologist.[8] Thyroid FNAs that did not fit into benign, suspicious or malignant categories were included in this category. In our study one case (0.9%) was identified as AUS, as shown in Fig. 1, for which repeat FNA was advised as per TBSRTC. In this study four cases (3.6%) were diagnosed as SFN on cytology. All 4 cases were obtained for histopathological study of which one case showed features of follicular carcinoma, another case showed features of follicular variant of papillary carcinoma, while the remaining two showed features of follicular adenoma similar to study by Renuka et al.[11]
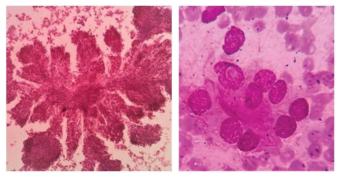

Fig. 1(A): Thyroid follicular cells arranged. **Fig. 1(B):** Intranuclear inclusion noted in papillae (smear, H&E stain, x10) (smear, Leishman stain, x40).
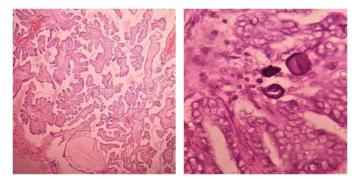

Fig. 1 (C): Section showing papillae. **Fig. 1(D):** follicular cells showing Orphan-Annie with fibrovascular core(H&E, x4) nuclei and psammoma bodies (H&E, x40).

The category follicular neoplasm or suspicious for a FN (FN/SFN): Cases which showed features of significant alteration in the follicular cell architecture, characterized by cell crowding, micro follicles, dispersed isolate cells and scant or absent colloid were diagnosed under this category, in this study four cases (3.6%) were diagnosed as SFN on cytology. All 4 cases were obtained for histopathological study of which 2 cases showed features of follicular carcinoma and follicular variant of papillary carcinoma, while the remaining two showed features of follicular adenoma similar to study by Renuka et al.[11]

In the category of suspicious for malignancy, we had 4 (3.6%) cases. We reported 04 cases under this category as suspicious for papillary carcinoma on FNA which predominantly had follicular pattern, and the nuclear features were subtle, specimen was obtained in all the 04 cases and were diagnosed as papillary carcinoma. TBSRTC recommends near-total thyroidectomy or surgical lobectomy for cases in this category. Studies done by Ko et al, and Kessler et al. had cases ranging from 2.2%–16.1%.[13,14]

In the category of malignant we had 08 cases, for which specimen was obtained in 04 cases, of which 03 cases were papillary carcinoma, the cytomorphology was as shown in Fig. 1(A,B), Fig. 1(C,D) showing the histopathology of the same and 01 case was medullary carcinoma the cytomorphology of which was as shown in Fig. 2(A,B), the histopathology being as in Fig. 2(C,D).
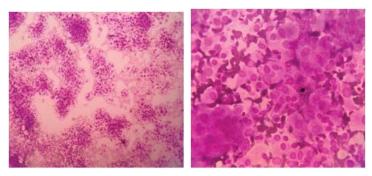

Fig. 2(A): Follicular cells arranged inclusters. **Fig. 2(B):** Individual cells are plasmacytoid and and singles(H&E, x4)show pleomorphism (H&E, x4).
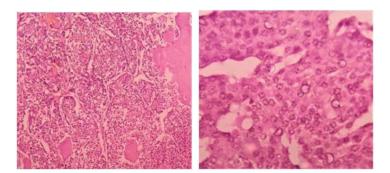

Fig 2 (C): Tumour cells arranged in nests, **Fig. 2(D):** Tumour cells show finely stippled to follicles and cords. Stroma shows amyloidcoarsely clumped chromatin (H&E, x40) deposits. (H&E, x10)

Conclusion

The Bethesda System for Reporting Thyroid Cytopathology is an excellent method of reporting thyroid FNA. It appropriately triages patients for management, and provides for a system of reporting where the clinician is guided by cytological findings in an unambiguous way. Under the category of SFN/FN there is some confusion in the clinical course to be taken, though it is always better to err on the side of caution. TBSRTC is a valuable step toward uniformity of reporting thyroid FNA. Interpretation and the adoption of this system will reap many benefits, not only in current medical practice by improving communication but also in future care. Universal application of TBSRTC may improve

inter-laboratory agreement and lead to consistent management approach, as it appraises the surgeon with guidelines for adequacy of samples, and interpretation of FNA reports and aids them in surgical decision making

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