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Original Research Article

Risk Stratification of Thyroid Cytology Specimens by Bethesda Reporting System: An Institutional Experience

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Abstract

Background & Objective: The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) is a universally accepted and standardized system to categorize thyroid fine needle aspiration (FNA) smears in patients with thyroid nodules. The system assigns a malignancy risk and gives recommendations for patient management in each category. The objective of the current study was to analyze the thyroid FNA by the Bethesda system, to correlate the cytopathology with histopathology and to assess the risk of malignancy in each category.

Methods: The current study was conducted on 324 retrospective cases of FNA smears of thyroid nodules over a period of two years from October 2017 to September 2019. Cytohistopathological correlation was observed in 52 cases. Subsequently, cytomorphological features were further classified according to TBSRTC into six groups, and correlated with clinico-histopathological features along with assessment of risk of malignancy.

Results: Diagnostic sensitivity and specificity of FNAC was 62.51% and 100%, respectively. The positive predictive value was 100% and negative predictive value was 92.6%. The number of cases in each diagnostic category and the risk of malignancy (ROM) were as follows: nondiagnostic – three cases (ROM – 0%), benign – 33 cases (ROM – 3.03%), atypia of undetermined significance – one case (ROM – 0%), follicular neoplasm – 3 cases (ROM – 33.33%), suspicious for malignancy – 2 cases and malignant – 4 cases (ROM – 100%) in both.

Conclusion: The Bethesda System is a uniform and effective modality in diagnosis and planning management of patients with thyroid gland lesions. Risk based stratification may guide the clinicians towards a more comprehensive approach to patient management.

Keywords: Bethesda system; Thyroid nodules; Follicular neoplasm.

Introduction

Thyroid cancer is one of the most evolving common endocrine malignancies, constituting 0.1%–0.2% of all cancers in India.[1] Fine-needle aspiration cytology (FNAC) is the foremost diagnostic procedure for evaluation of thyroid nodules and its role in prognosis and management has been well established.[2]

A standardized system of reporting thyroid cytopathology specimens was introduced in the year 2007; The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) with a revised criteria given in 2017 in an attempt to categorize morphological criteria in fine-needle aspirations (FNAs) from patients with thyroid nodules.[2] TBSRTC establishes six diagnostic criteria for results of thyroid FNA's: (i) nondiagnostic

or unsatisfactory; (ii) benign; (iii) atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS); (iv) follicular neoplasm or suspicious for a follicular neoplasm (FN/SFN); (v) suspicious for malignancy (SFM); and (vi) malignant.[3] The system assigns a malignancy risk and gives recommendations for patient management in each category.[2] TBSRTC is a widely used reporting system and studies worldwide have concluded that it reduces the use of unnecessary thyroid surgeries while also ensuring the quality of thyroid malignancy detection.[4]

The objective of the present study was to analyze the thyroid cytology smears in our institution by the Bethesda system, to correlate the cytopathology with histopathology wherever surgery was done and to assess the risk of malignancy in each category.

Material and Methods

The current study was conducted on 324 cases of thyroid swelling who underwent FNAC in the Department of Pathology, IIMS&R, Lucknow (UP), retrospectively for a period of two years from October 2017 to September 2019. The patients age ranged from 12 to 85 years with a mean of 38 years. Detailed clinical history and results of local and general examination was noted in each case. Out of 324 cases, cyto-histopathological correlation was observed in 52 cases where surgery was performed.

FNAC procedure in our institute is performed using 10 mL disposable syringes and 23-G needles after taking informed consent from each patient. The gross appearance of aspirate is noted and smeared on clean glass slides. FNA dried smears are stained with May– Grunwald-Giemsa staining technique and wet smears fixed in 95% ethanol are stained with haematoxylin and eosin (H&E) stain and Papanicolaou stain as per the standard protocol. The cytological features of the smears were evaluated retrospectively and reporting was done based on the morphologic criteria given by the Bethesda reporting system. The slides were reviewed by two pathologists in a blinded fashion. The six categories are (1) nondiagnostic/ unsatisfactory (ND/UNS), (2) benign, (3) atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS), (4) follicular neoplasm (FN) or suspicious for FN (SFN), (5) suspicious for malignancy (SFM), and (6) malignant.

H&E stained histopathological specimens in cases wherever available were analysed to correlate with. The histopathological diagnosis was considered as the gold standard to assess sensitivity, specificity and diagnostic accuracy.

Statistical Analysis

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy was analysed with SPSS version 11.0. Risk of malignancy (ROM) for each cytological category based on Bethesda system was calculated as the number of malignant neoplasms divided by the total number of the cases in a given category.[2]

Results

The current study analyzed 324 cases of thyroid lesions in a period of two years from October 2017 to September 2019. The age range for all thyroid lesions was 12 to 85 years with a mean age of 38 years. Overall female to male ratio was 7.5:1. The distribution of cases into the categories based on Bethesda reporting system is given in Table 1.

Of the 324 cases undergoing FNAC, the largest burden was of the benign lesions with 284 cases (87.6%). There were 8 cases (2.5%) reported to be malignant and 2 cases (0.6%) signed out as suspicious for malignancy. The category AUS/ FLUS included only a single case (0.3%) while there were 5 cases (1.5%) in category FN/SFN. 24 cases (7.4%) were reported to be non diagnostic.

Out of the total 324 cases, only 52 cases could could be followed up histopathologically. Their distribution and subsequent risk of malignancy has been given in Table 2. Surgical specimens of 3 cases, 33 cases, and 1 case, respectively, for categories ND/UNS, benign, and AUS/FLUS were received. Nodular goitre was the predominant diagnosis followed by lymphocytic thyroiditis, granulomatous thyroiditis and one case was diagnosed as papillary thyroid carcinoma. Our observations revealed a nil risk of malignancy in the non diagnostic and AUS/FLUS category.For nodules with benign FNA cytology there was a low risk of malignancy (3.03%). Of 15 cases of FN/SFN, SFM, and malignant category, 9 were surgically resected. Among the 3 cases of FN/SFN, 2 were benign (follicular adenoma) and 1 was malignant (follicular carcinoma). Papillary thyroid carcinoma was reported in 2 cases of suspicious for malignancy. Out of the 4 cases of malignancy papillary thyroid carcinoma was reported in 2 cases, medullary

Table 1: Distribution of cases according to the Bethesda System for Reporting Thyroid Cytopathology.

Cytological Category	Number of Cases	Percentage
1. Nondiagnostic / unsatisfactory (ND/UNS)	24	7.4
2. Benign	284	87.6
i. Consistent with benign follicularnodule (includes adenomatoidnodule, colloid nodule, etc.)	250	
ii. Consistent with lymphocytic(Hashimoto) thyroiditis	30	
iii. Consistent with granulomatous (subacute) thyroiditis	4	
iv. Others		
3. Atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS)	1	0.3
4. Follicular neoplasm/suspicious for a follicular neoplasm (FN/SFN) including Hurthle cell neoplasm	5	1.5
5. Suspicious for malignancy (SFM)	2	0.6
i. Suspicious for papillary carcinoma	2	
ii. Suspicious for medullary carcinoma	0	
iii. Suspicious for metastatic carcinoma	0	
iv. Suspicious for lymphoma	0	
v. Others	0	
6. Malignant	8	2.5
i. Papillary thyroid carcinoma	5	
ii. Poorly differentiated carcinoma	0	
iii. Medullary thyroid carcinoma	2	
iv. Undifferentiated (anaplastic)carcinoma	1	
v. Squamous cell carcinoma	0	
vi. Carcinoma with mixed features	0	
vii. Metastatic carcinoma	0	
viii. Non-Hodgkin lymphoma	0	
ix. Others	0	
Total	324	100

Table 2: Cytohistological Correlation in the Study Cases.

Cytological Category	Number of Cases where Surgical Specimens were received (n = 46)	Histopathological Diagnosis	Risk of Malignancy (%)
ND/UNS (n = 24)	3	Nodular goitre (3)	0
Benign (n = 284)	33	Nodular goitre (24) Lymphocytic thyroiditis (6) Granulomatous thyroiditis (2) Papillary thyroid carcinoma (1)	3.03
AUS/FLUS (n = 1)	1	Nodular goitre (1)	0
FN/SFN (n = 5)	3	Follicular adenoma (2) Follicular carcinoma (1)	33.33
SFM (n = 2)	2	Papillary thyroid carcinoma (2)	100
Malignant (n = 8)	4	Papillary thyroid carcinoma (2) Medullary thyroid carcinoma (1) Anaplastic thyroid carcinoma (1)	100

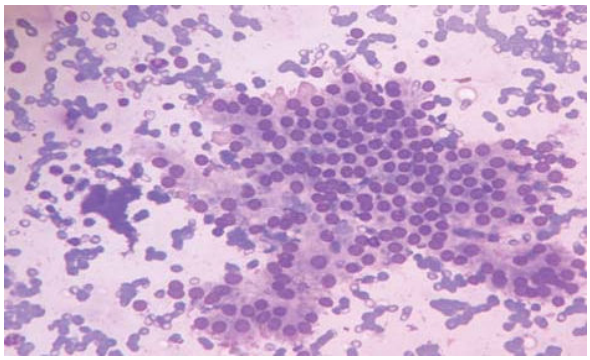

Fig. 1: Benign follicular nodule. Photomicrograph showing monolayered sheets of evenly spaced follicular cells having a honeycomb like arrangement along with fire flares (MGG stain, ×40).

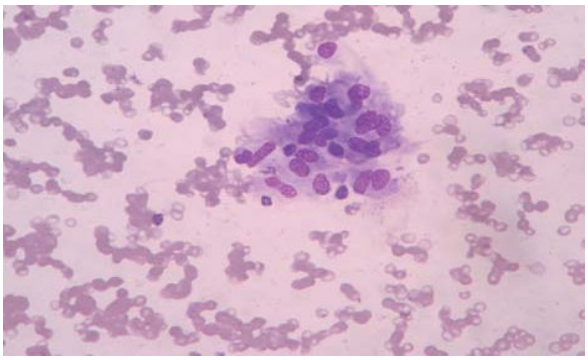

Fig. 2: Photomicrograph of granulomatous thyroiditis : fine needle aspiration thyroid smears showing clusters of epithelioid histiocytes mixed with benign follicular cells (MGG stain, ×40).

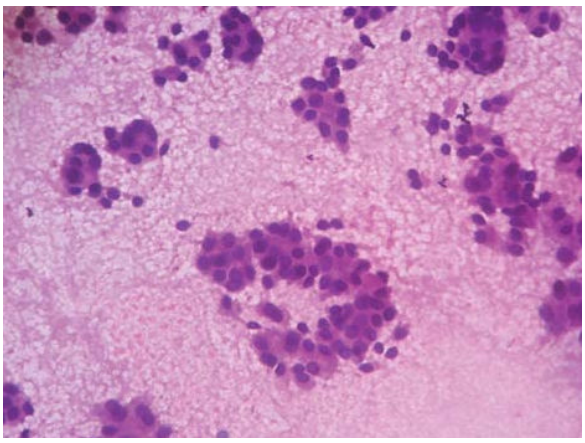

Fig. 3: Photomicrograph showing follicular neoplasm: a cellular aspirate composed of uniform follicular cells arranged in crowded clusters and microfollicles (MGG stain, × 40).

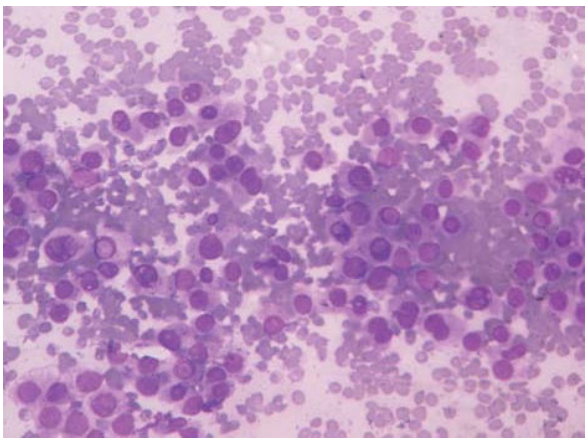

Fig. 4: Photomicrograph of FNA thyroid smears showing papillary thyroid carcinoma composed of cells with fine powdery chromatin, micronucleoli, and intranuclear cytoplasmic pseudoinclusions (MGG stain, × 40).

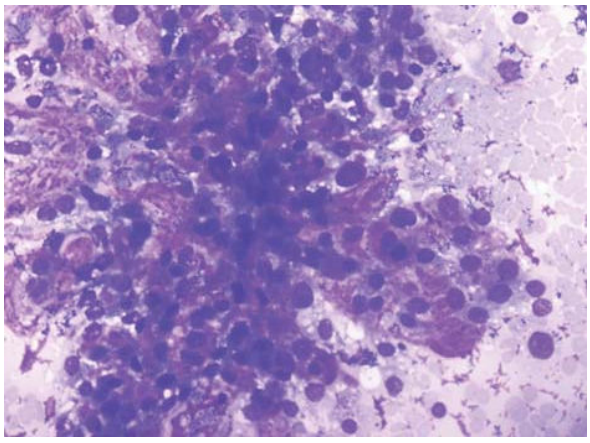

Fig. 5: Photomicrograph showing medullary thyroid carcinoma displaying dispersed plasmacytoid cells with variation in nuclear size and shape and amyloid in the background (MGG stain, × 40).

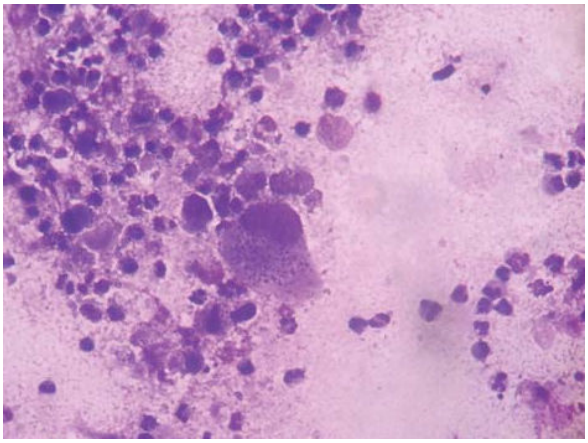

Fig. 6: Photomicrograph of fine needle aspiration thyroid smears showing anaplastic thyroid carcinoma displaying dispersed cells with marked pleomorphism (MGG stain, × 40).

carcinoma and anaplastic carcinoma in 1 case each. Nodules with frankly malignant cytologic patterns undergoing surgery were all invariably cancer on histopathology. The risk of malignancy was 33.33% in the follicular neoplasm category and 100% in the SFM group.

Diagnostic sensitivity and specificity of FNAC for the thyroid gland lesions was 62.51% and 100%, respectively. The PPV was 100% and NPV was 92.6%.

Discussion

The role of FNAC to diagnose thyroid lesions has been well established as a safe, cost-efficient, minimally invasive procedure and an aid to the clinicians in the planning of management.[5,6] The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) is a standardized, widely accepted and category based reporting system for thyroid cytology specimens.[5] The management protocol is based on the category labelled. For instance surgery is not recommended for ND/UNS, benign, and AUS/FLUS categories. Instead repeat FNA or clinical follow up is advised.[7] Whereas the higher categories are followed up with surgical management. We as pathologists have a role to render anaccurate and understandable diagnoses, so as to guide the clinicians towards a correct interventional strategy. The assessment of the risk of malignancy in thyroid lesions is equally important and has been widely studied following their classification into the Bethesda category.[8-10]

In the current study on 324 FNAC specimens of thyroid gland lesions, 7.4% cases were in the non diagnostic category. The subcategories include cyst fluid only, virtually acellular specimen and

other factors (obscuring blood, clotting artefact, etc.). Other recent studies have recorded 1.2% to 16.4% cases in this group.[7-14] The Bethesda system advocates these lesions to be re-aspirated after a minimum period of 3 months to prevent false positive cases owing to reparative or reactive changes.[3] Our observations revealed a nil risk of malignancy in the non diagnostic category. Three histopathological specimens were received owing to high index of suspicion and both were nodular goitre. The low number of surgeries in this category could suggest a confounding factor for the nil risk of malignancy.

Our study revealed 87.6% cases to be in the "benign'' category. The range of cases in this category has been studied to be 34% to 87.5% in previous studies.[7-14] Very few studies claim to have a rate lower than 60% and that too due to a high incidence of AUS/FLUS and FN/SFN. [13] Nodular goitre was the predominant diagnosis followed by lymphocytic thyroiditis, granulomatous thyroiditis and one case was diagnosed as papillary thyroid carcinoma following surgery. The risk of malignancy in this category was observed to be 3.03% which is similar to other studies.[3,8]

In the category AUS/FLUS, specimens contained cells with architectural and/or nuclear atypia but not to the extent as to be classified as suspicious for malignancy. In our study we had only one case over a period of two years and it was followed up to be benign post operatively. Molecular tests are being recommended to lower the incidence in this group.[14] Other studies have also reported a low incidence in this group.[7-14] The risk of malignancy has been established to be 5–15% in this group by the Bethesda system.[2] We however reported a 0% risk probably because of the low incidence of reporting of this category.

The category (FN/SFN) including Hurthle cell neoplasm had a 1.5% incidence in our study. Previous studies have shown a range between 2.2–16.1% cases in this group.[7-14] Surgical follow up revealed 2 cases of follicular adenoma and 1 case of follicular carcinoma. The ROM was approximately 33% which was close to other studies.[2,13] An indeterminate microfollicular cytology pattern in the absence of nuclear atypia is associated with a low risk of malignancy and may be managed conservatively with observation. In contrast, cytologic nuclear atypia consistent with a follicular neoplasm confers a high risk of cancer and requires aggressive management.[8]

We reported only 2 cases of SFM category and both were surgically followed up to be papillary thyroid carcinoma. Articles have mentioned a very high risk of malignancy in this category and it corroborates our data as well.[2,8,13]

The malignant category had a range of 2.9% to 11% in recent studies.[7-14] Our study had 8 (2.5%) cases in this category. Four cases from this category diagnosed as "malignant" on cytology underwent surgery. Two of them were diagnosed as PTC on histopathology, one case was diagnosed as medullary carcinoma and one case as anaplastic carcinoma. The cytologic diagnoses of frank malignancy, especially papillary carcinoma, is highly reliable, and thus may be used as a guide for planning surgery appropriate for thyroid cancer.[8] The ROM as high as nearly 100% has been evidenced by other studies as well.

The statistical parameters reported in our study were a sensitivity and specificity of 62.51% and 100%, respectively for FNAC of the thyroid gland lesions followed by histopathology. The PPV was 100% and NPV was 92.6%. Recent studies have published similar results.[6,7]

Conclusion

In conclusion, the current study highlighted the utility of The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) as a uniform and highly effective modality in diagnosis and planning management of patients with thyroid gland lesions. Risk based stratification may guide the clinicians towards a more comprehensive approach to patient management. Next generation molecular studies may further refine FNA diagnosis in the cytologically indeterminate group where there is high variability in interobserver histopathological diagnosis.

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