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Original Research Article

Cytopathological evaluation of various thyroid lesions based on Bethesda system for reporting thyroid lesions

Ashwini S. Khadatkar*, Varsha M. Dhume, Vikas Kavishwar

Department of Pathology, Topiwala National Medical College and B. Y. L. Nair Hospital, Mumbai, Maharashtra, India

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***Correspondence:**
Dr. Ashwini S. Khadatkar,
E-mail: drashwini5apr@gmail.com

ABSTRACT

Background: An encouragement for the thyroid proposal was the Bethesda system for reporting cervical cytology interpretations, a uniform reporting system for thyroid FNA will facilitate effective communication among health care providers. The objective of the present study was to classify thyroid lesions in various categories under Bethesda system correlating the cytological findings in various thyroid lesions with clinical and radiological details.
Methods: A retrospective study on FNAC thyroid was performed in a tertiary hospital and a Medical teaching institution in Mumbai, Maharashtra, India which included cases which were reported from 1st January 2010 to 31st July 2011. For cytomorphological analysis, all smears (Papanicolaou and MGG) were reviewed and cases were categorized into six Bethesda categories. The FNAC findings were correlated with clinical, radiological and laboratory findings. Discrepancies between original diagnosis and review diagnosis as well as difficulties encountered during application of Bethesda were studied in detail.
Results: Total 413 FNACs were received during the study period. The original diagnoses included 10 different categories or labels some of which were descriptive. On application of Bethesda, maximum cases were found in category II (82.32%) followed by category I i.e. inadequate (7.7%). Category III (Atypia of Undetermined significance) included wide spectrum of cases which were previously diagnosed as goitre, suspicious or neoplastic.
Conclusions: Bethesda system of reporting thyroid FNAC has brought uniformity in cytology reporting. It has facilitated better understanding between cytopathologist and clinicians as every category connotes specific risk of malignancy and recommends treatment.

Keywords: AUS category, Benign and malignant lesions, Bethesda system, FNAC

INTRODUCTION

The thyroid gland is the largest endocrine organ which plays vital role in body metabolism. Both non-neoplastic and neoplastic diseases affect it and lead to diffuse or nodular enlargement. Non-neoplastic lesions are more common in thyroid like goitre, thyroiditis and graves' disease.[1] Neoplastic lesions like follicular neoplasms, papillary carcinoma, and medullary carcinoma though less common may show overlapping clinical features with non-neoplastic lesions. There are various diagnostic modalities to work up thyroid diseases which include thyroid function tests, radioisotope scan, USG, AMA levels and FNAC. FNAC is considered the gold standard diagnostic test in the evaluation of a thyroid nodule, and other tests like ultrasound and nuclear scan should be used in conjunction with FNAC.[2]

More than 50% of the world's population harbours at least a thyroid nodule and the frequency of thyroid diseases increases with age.[3] It is therefore not a surprise that thyroid fine needle aspiration (FNA) is one of the most commonly practiced areas in cytopathology. Despite the frequent occurrence of the thyroid nodules, the majority 95% of them are benign.[4] The critical issue in the management of patients with thyroid disease is to find a way to distinguish preoperatively benign nodules (the overwhelming majority) from cancers (the minority cases). Radiological, serological and molecular studies have made major improvements in the diagnosis and management of patients with thyroid disease.

Numerous studies have proven the tremendous impact of thyroid FNA in care of patients with thyroid disease. The entire current management approach for patients with thyroid disease hinges upon a cytopathological diagnosis. Triaging of patients with thyroid disease who are to be surgically managed has become more accurate recent years, due to an optimum use of thyroid FNA and better understanding of the cytomorphological characteristics of thyroid disease. To address the terminology and other issues related to thyroid FNA, The National Cancer Institute NCI hosted the NCI thyroid fine needle aspiration state of the science conference.

An encouragement for the thyroid proposal was the Bethesda system for reporting cervical cytology interpretations, first developed at an NCI workshop in 1988 and widely accepted in the United States for reporting Papanicolaou test results. A uniform reporting system for thyroid FNA will facilitate effective communication among cytopathologists, endocrinologist, surgeons, radiologists and other health care providers. It will also facilitate cytologic-histologic correlation for thyroid diseases. It will help in research on the epidemiology, molecular biology, pathology and diagnosis of thyroid diseases, particularly neoplasia and allow easy and reliable sharing of data from different laboratories for national and interventional collaborative studies.

The objectives of the present analysis were to study cytological findings in various thyroid lesions and to classify thyroid lesions in various categories under Bethesda system. The objectives also were focused to correlate the cytological findings in various thyroid lesions with clinical and radiological details. Comparative analysis between original cytological diagnosis and review diagnosis was also performed.

METHODS

A retrospective study on FNAC thyroid was performed in a tertiary care hospital. These included FNACs performed from 1st January 2010 till 31st July 2011.

The data and cytology smears were retrieved from old records for review. Clinical, USG, thyroid function tests, antithyroid antibody tests and Tc99 scan and cytology findings were noted in these cases. All cytology smears (Papanicolaou and MGG) were reviewed by three independent observers and were classified as per Bethesda classification. Relative frequencies of cases in each Bethesda categories were noted. The original diagnosis (pre-Bethesda) and review diagnosis were compared and discrepancies in two diagnoses and difficulties encountered during classification were studied in detail.

RESULTS

Total 413 FNACs were reviewed. Majority of cases were in age group of 3rd to 5th decade and showed female preponderance. Among the presentations MNG was the commonest (45.8%) followed by diffuse (37.47%). Among the functional status, euthyroid were maximum (54.2%) followed by hyperthyroid. AMA and Tc scan was available in 52 and 48 cases respectively, AMA 34 cases had positive values and 42 cases scan had increased uptake.

Reviewed diagnosis after applying Bethesda categories:

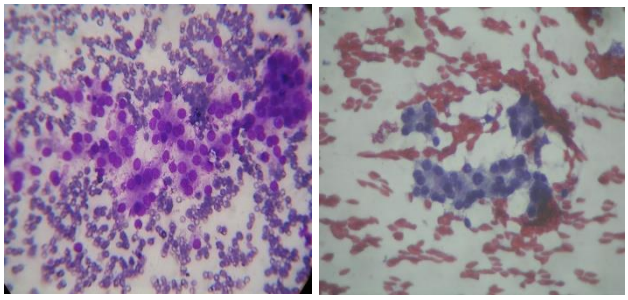

Figure 1: MGG stained cytology smear on left shows thyroid follicular cells arranged in follicular pattern and shows fire flares. (Bethesda category II) on right, pap stained smear shows thyroid follicular cells in clusters and follicles with no colloidal background (Bethesda category IV).

Table 1: Pre-Bethesda (previous diagnosis): n= 413.

Pre-Bethesda diagnosis	Number of cases
Inadequate	06 (1.45%)
Benign descriptive	04 (0.96%)
Goitre	277 (67.07%)
Lymphocytic thyroiditis	65 (15.73%)
Hyperplastic goitre	23 (5.5%)
Suspicious of malignancy	08 (1.9%)
Suspicious of follicular neoplasm	01 (0.24%)
Follicular neoplasm	05 (1.21%)
Hurthle cell neoplasm	01 (0.24%)
Malignancy	23 (5.56%)
Total(n)	413

Table 2: Distribution of cases under Bethesda categories.

Bethesda category	I	II	III	IV	V	VI	Total
No. of cases	32 (7.7%)	340 (82.32%)	13 (3.1%)	06 (1.45%)	00 (00%)	22 (5.3%)	413

Table 3: Comparison between original diagnosis and review diagnosis (N= 413).

Pre-Bethesada	Number of cases	Review diagnosis	Number	Bethesda categories
Inadequate	06 (1.45%)	Inadequate	06	Cat I
Benign descriptive	04 (0.96%)	1) Inadequate	01	Cat I
		2) Goitre	03	Cat II
Goitre	277 (67.07%)	1) Inadequate	26	Cat I
		2) Goitre	246	Cat II
		3) Thyroiditis	02	Cat II
		4) AUS	03	Cat III
Lymphocytic thyroiditis	65 (15.75%)	1) Inadequate	01	Cat I
		2) Thyroiditis	64	Cat II
Hyperplastic goitre	23 (5.5%)	Hyperplastic goitre	23	Cat II
Suspicious of malignancy	08 (1.9%)	1) AUS	07	Cat III
		2) Pap CA	01	Cat VI
Suspicious of follicular neoplasm	01 (0.25%)	Follicular neoplasm	01	Cat IV
Follicular neoplasm	05 (1.21%)	1) AUS	01	Cat III
		2) Follicular neoplasm	04	Cat IV
Hurthle cell neoplasm	01 (0.24%)	Hurthle cell neoplasm	01	Cat IV
Malignancy	23 (5.56%)	AUS	01	Cat III
		Malignancy	22	Cat VI
Total (n)	413			

DISCUSSION

From January, 2010 to June, 2011, 413 thyroid FNAC cases were received in the department of cytology of a tertiary teaching institute. These cases were originally reported as per existing reporting system which included descriptive terminologies. These cases were retrieved and cases were classified retrospectively into various Bethesda categories.

The bulk of thyroid diseases are frequently encountered in young and middle aged groups with majority of patients being females in reproductive age groups. In present study, the age distribution ranged from 1st decade to 9th decade and maximum no. of cases were in the age group 30-50 years. A female preponderance was noted in our study with 338 (82.62%) cases. Similar female preponderance was noted by Unnikrishnan et al.[9]

As reported by Tsegaye et al 85.7% per cent of the thyroid diseases were found in the age group 20-59 years.[10] In present study, 71.51% cases were in the similar age group.

In present study thyroid function tests were done on 321 cases (77.86%). Out of which 24.5% were hyperthyroid, 20.9% were hypothyroid and 54.2% were euthyroid, which was found to be variable as compared to reports given by Mandakini et al.[11]

Combining USG and clinical presentations, cases were classified as MNG, Diffuse and STN. In the present study, MNG were 45.8%, Diffuse 37.47%, STN 16.69%. In study by Mandakini et al majority of thyroid lesions (117) were nodular followed by diffuse swelling which was noted in 77 cases whereas in present study, MNG were seen in the majority of cases followed by diffuse.[11]

In pre-Bethesda group, the original cytological diagnoses could be summed up in 10 categories as depicted in Table 1. It included categories such as Inadequate (1.45%), Benign descriptive (0.96%), goitre (67.07%), Lymphocytic thyroiditis (15.73%), hyperplastic goitre (5.5%), suspicious of malignancy (1.9%), suspicious of follicular neoplasm (0.24%), follicular neoplasm (1.21%), hurthle cell neoplasm (0.24%), malignancy (5.56%). Majority of the diagnostic labels used were broad and descriptive. They did not imply any specific treatment modalities. Such reports created confusion for treating clinicians and affected patient care.

After applying Bethesda to the same cases (413), they were categorised as six categories as summed up in Table 2. I (7.7%), II (82.3%), III (3.1%), IV (1.45%), V (0%),

and VI (5.3%). Jo et al conducted study of 3,080 thyroid FNA samples from 1992 to 2009, at the University of Virginia Health System, Charlottesville, and classified thyroid lesions according to TBSRTC. Of the 3,080 FNAC samples, 18.6% were non-diagnostic, 59.0% were benign, 3.4% were atypical follicular lesion of undetermined significance (AFLUS), 9.7% were "suspicious" for follicular neoplasm (SFN), 2.3% were suspicious for malignancy (SM), and 7.0% were malignant.[6] Higher percentage of benign lesions was observed in our study as compared to study by Jo et al, this could be attributable to geographical variation.[6] Various workers were also reported similar results to our results.[7,8]

On comparing original and review diagnoses, discrepancies in diagnosis was observed in 41 cases amounting 9.9%. In pre-Bethesda group, the original cytological diagnoses had maximum number of goiters, lymphocytic thyroiditis, and hyperplastic goiters all together amounting to 88.93% benign lesions. Even after applying Bethesda, maximum cases were classified as category II benign lesions (82.3%). On applying Bethesda, majority of benign lesions like goiter, thyroiditis, and hyperplastic goiter were classified as category II i.e. benign however 28 cases were classified as category I i.e. Inadequate. Thus, major reason for interobserver variation in these cases was related to strict application of adequacy criteria as stated in Bethesda system.

Another variation noted was 3 cases of goiter which were reported as a newly categorized of AUS (category III). The cases which show atypical features like nuclear pallor, nucleoli and grooves in few cells in a cellular smear or sparsely cellular smear with atypical features cannot be directly labelled as suspicious of malignancy or malignancy and such indeterminate cases were placed in category III of AUS by Bethesda system. The probable reasons for this change from benign to category III on review was sparsely cellular blood mixed smears, scant thin colloid and few cells with enlarged nuclei and presence of nucleoli.

Majority of cases which were labelled as suspicious of malignancy (8 cases) on original diagnosis were categorized as AUS in 7 cases and a sole case was diagnosed as papillary carcinoma. Here these were put in AUS category as these cases showed sparse cellularity, atypical cells with enlarged pale nuclei and occasional grooves along with few cell clusters with benign features. These features were not enough to label them as suspicious of malignancy or malignant. Similar insufficient atypical features were observed while categorizing 2 cases of follicular neoplasm and one case of malignancy as AUS.

Ideally cases of AUS need a close follow up with a repeat FNA after 3 months as per Bethesda recommendations whereas near total/ total thyroidectomy is recommended for category V and VI. Significant interobserver variabilities have been reported in making diagnosis of AUS. The use of representative case materials, use of consensus review with cytological histological correlation and providing individual feedback through quality assurance metrics and continuous educational sessions may help to improve the performance.[5]

Summarizing all, there was not a great difference in Pre-Bethesda and review diagnosis while classifying a lesion as benign or malignant. However, 12 cases were classified as AUS and 28 were classified as inadequate. Both these groups warranted a repeat FNAC after a period of 3 months to yield a more definitive diagnosis. Nayar and Ivanovic et al analyzed 1150 thyroid FNA samples with application of Bethesda system.[12] They concluded that a 6-tier reporting system for thyroid FNAC was effective for determining which patients needed surgery versus follow up FNA and also guided clinician on the extent of surgery.

Use of new standardized nomenclature as recommended by Bethesda has led to improved interobserver and inter institutional reproducibility. It has been readily accepted by the clinicians and has resulted in better and consistent management approach. In our experience, Bethesda had better ability to define malignant lesion or the lesions which may require surgical intervention.

The controversial area in Bethesda classification is newly introduced category III i.e. atypia of undetermined significance. It represents heterogeneous group of FNAC patterns where definitive diagnosis cannot be given. Its use has been subject of controversy as this category shows fair to poor reproducibility and marked inter institutional variation. Bethesda has recommended its judicial use with careful monitoring. Some authors propose use 5 tired system with combined category encompassing AUS as well as SFN lesions. However, AUS covers wide variety of diagnostic possibilities as compared to follicular neoplasm group. Though risk of malignancy reported in these groups is more or less similar; type of malignancy differs. AUS is often associated with underlying papillary carcinoma whereas SFN group is associated with follicular carcinoma. Management approach may differ for these two categories of malignancy.

CONCLUSION

The Bethesda system provides a standardized nomenclature for thyroid cytopathology reporting with improved interobserver reproducibility. It results in better understanding of cytology reports by clinicians and helps in better and consistent management approach especially in selecting cases which may require surgical intervention.

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