



FNAC of Thyroid Lesions Based on Bethesda System: A Retrospective Cytological Study in a Tertiary Care Centre in North India

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Abstract

Introduction: FNAC of thyroid lesions based on the Bethesda system, a six-category scheme represents a major step towards a uniform reporting system for thyroid. **Aim:** The aim of the present study was to determine the frequency rates of diagnostic categories of Bethesda system and to assess its accuracy when compared with histopathological diagnosis, wherever available and comparison of results with previous studies.

Material and Methods: This is a 1-year retrospective study of 150 patients with thyroid swelling from June 2019 to July 2020, conducted in the Cytology Section of the Department of Pathology, Govt. Medical College, Jammu. **Results:** Out of total 150 patients the maximum number of cases i.e., 127 were benign (Category 2) followed by 10 cases as Non-diagnostic (Category 1), 5 cases as malignant (Category 6), 4 cases were of suspicious for follicular neoplasm (Category 4) and 2 cases each of Category 3 and Category 5. Colloid Goitre cases were 90 followed by 27 cases of Lymphocytic Thyroiditis. In Category 6 i.e., Malignant, 3 cases were of Papillary Carcinoma. Histopathological diagnosis was available in 21 cases only and all the malignant diagnosis given on cytology were malignant on histopathology also. **Conclusion:** FNAC is rapid, simple, and safe diagnostic modality used as an excellent first line method for investigating the nature of lesion. Bethesda for thyroid is a simplified and standardized system, which provides better communication between cytopathologist and clinicians for better patient management protocol.

Key Words

Fine Needle Aspiration Cytology (FNAC), Thyroid Lesions, The Bethesda System for Reporting Thyroid Cytology (TBSRTC)

Introduction

Thyroid FNAC has an impact in the clinical management of a patient with thyroid pathology. Thyroid is one of the largest endocrine organs and both non-neoplastic and neoplastic abnormalities are a frequent source of specimens for surgical pathology laboratories. Thyroid nodules are highly prevalent and require cytopathological evaluation. Every patient with a palpable thyroid nodule is a candidate for FNAC. The major concern in persons who present with thyroid nodules is

the possibility of a malignant neoplasm. Majority of thyroid nodules prove to be localised, non-neoplastic. Benign neoplasms outnumber the thyroid carcinomas by a ratio of 10:1 (1). Thyroid swellings are clinically significant as about 42 million people in India suffer from thyroid diseases (2). Less than 5% of all nodular swellings of thyroid are documented as malignant (3). The incidence of thyroid cancer is increasing worldwide and such an

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increase is attributed to the phenomenon of over-diagnosis. Thyroid cancer is the fifth most common cancer in women. The number of new cases in women in their twenties is 5 times higher than for men in their twenties.

FNAC of thyroid is the most reliable and cost-effective diagnostic modality, however due to lack of a standardized terminology, diagnostic categories were defined differently among institutions thus confusing clinicians and inconsistent patient management. Bethesda System, proposed by National Cancer Institute, at a conference in Bethesda U.S in 2007 represents a major step towards a uniform reporting system for thyroid, is useful for both clinicians and pathologists. Each category with an implied malignancy risk that links it to rational clinical management guidelines (4). FNAC provide highly accurate cytologic information from which definitive management plan could be arranged with high sensitivity and specificity approaching to 96% (5). In context to pros and cons of TBSRTC, the experiences have been published as commentary for proposed modifications and updates for the 2nd edition from an international panel in 2016 (6).

Material and Methods

Between June 2019 to July 2020 results of 150 thyroid aspirates (obtained by FNAC) were evaluated retrospectively in the Cytology Section of Department of Pathology, Govt. Medical College, Jammu, after taking clearance from the Institutional Ethical Committee. Thyroid aspirates were divided into six categories based on Bethesda system. Age of patient ranged from the youngest of 20 years to oldest of 70 years. Both May Grunwald Giemsa and Pap-stained slides were reviewed taking in account the necessary clinical details, laboratory values of T3, T4, TSH and ultrasonographic details from the cytology forms. Cytological and histopathological diagnosis of 21 thyroid swellings were available (who had undergone surgical excision after FNAC) were compared. Haematoxylin & Eosin-stained slides were reviewed for that.

Results

Out of 150 patients, majority (100) were females and 50 were males with a M:F ratio of 1:2. The youngest patient was a female of 20 years with Papillary Carcinoma thyroid and oldest of 70 years with Anaplastic Carcinoma Thyroid. Distribution of cases as per Bethesda Category system is given in *Table 1* and further distribution of Benign and Malignant lesions in *Table 2* & *3*. *Table 4* shows the distribution of Histopathological diagnosis of 21 cases who had undergone surgical excision after FNAC. All the 5 malignant cases diagnosed as

Bethesda Category 6 on FNAC, turned out to be malignant on Histopathological examination. 4 cases were diagnosed as follicular adenoma on HPE, out of which 2 were given as Atypia of Undetermined Significance (AUS) on cytology and 2 as suspicious for Follicular Neoplasms (Category 4). 1 case given as suspicious for malignancy (Category 5) turned out to be Papillary carcinoma on HPE. All the 11 cases given on cytology as Colloid Goitre turned out to be Colloid Goitre on HPE.

Table 1: Distribution of Cases as Per Bethesda Category System

Bethesda Category	No. of Cases	Percentage (%)
1. Non-Diagnostic	10	6.67
2. Benign	127	84.67
3. Atypia of Undetermined Significance (AUS)	02	1.33
4. Suspicious for Follicular Neoplasm (SFN)	04	2.67
5. Suspicious for Malignancy (SFM)	02	1.33
6. Malignant	05	3.33
Total	150	100

Table 2: Distribution of Benign Category Cases

Benign	No. of Cases	Percentage (%)
1. Colloid Goitre	90	70.86
2. Adenomatoid Goitre with Features of Hyperactivity	05	3.94
3. Lymphocytic Thyroiditis	27	21.26
4. DeQuervain Thyroiditis	05	3.94
Total	127	100

Table 3: Spectrum of Malignant Lesions

Malignancy	No. of Cases	Percentage (%)
1. Papillary Carcinoma	03	60
2. Medullary Carcinoma	01	20
3. Anaplastic Carcinoma	01	20
Total	05	100

Table 4: Correlation of Cytologic Diagnosis with Histopathological Diagnosis

Bethesda Category	Cytologic Diagnosis	No. of Cases with Available Histopathology	Histopathological Diagnosis
1. Non-Diagnostic	10	0	-
2. Benign	127	11	Colloid Goitre
3. AUS	02	02	Follicular Adenoma
4. SFN	04	02	Follicular Adenoma
5. SFM	02	01	Papillary Carcinoma
6. Malignant	05	05	Papillary-03, Medullary-01, Anaplastic-01

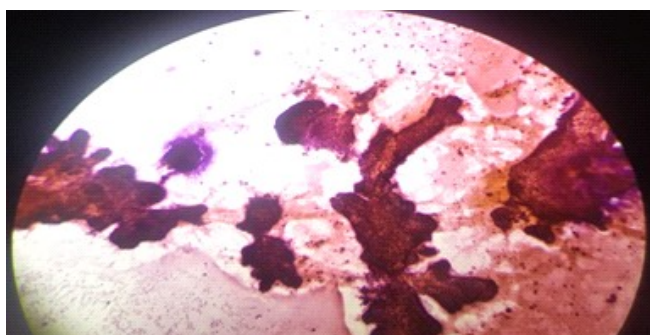


Figure 1: Atypia of Undetermined Significance (AUS) Showing Intact Papillary Fragments Without Showing Any Nuclear Features of Papillary Carcinoma

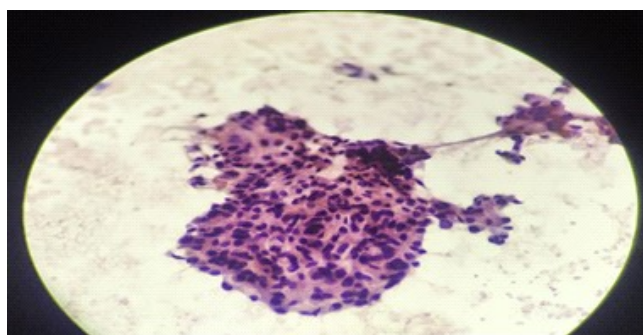


Figure 2: Photomicrograph Showing Lymphocytes Impinging on the Thyroid Follicular Epithelial Cells in a Case of Lymphocytic Thyroiditis

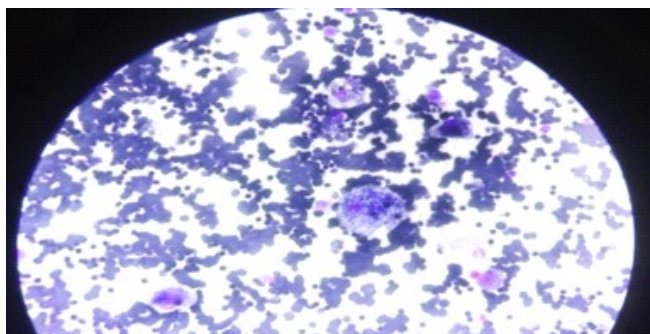


Figure 3: Photomicrograph Showing Cystic Macrophages in a Case of Colloid Goitre with Cystic Degeneration

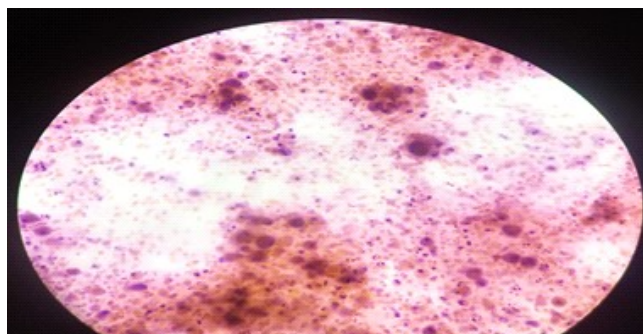


Figure 4: Pap-Stained Smear Showing Abundant Colloid and Cystic Macrophages in a Case of Colloid Goitre

Discussion

Early diagnosis of thyroid cancer is important due to low malignant potential of thyroid nodules and its slow progressive nature. Thyroid Bethesda system for reporting Thyroid Cytology (TBSRTC) has been widely adopted in the United States and worldwide endorsed by the American Thyroid Association. The studies on FNAC over nodular thyroid lesion have observed that, nodular thyroid pathology was maximally distributed in the age

group of 31-40 years (7,8).

Our study in 150 FNAC's showed 6.67% cases as Non-diagnostic (Category-1) due to obscuring blood, thick smears, air drying or inadequate sampling resulting from sclerotic, calcified nodule or in some cases lesion being deep required ultrasound guided assistance. This correlates with the study of Bhat *et al.* (9) and Mehra *et al.* (10). Benign category (Category-2) outnumbers all the other categories with 84.67% cases similar to the study of



Mondal *et al.* (11) and Gupta *et al.* (12). For a thyroid FNAC specimen to be satisfactory for evaluation, at least 6 groups of benign, well visualized follicular cells are required, each group composed of at least 10 cells. There are many exceptions like a specimen with abundant colloid is adequate (and benign) even if 6 groups of cells are not identified. Specimens that consist only of cyst contents (macrophages) are problematic. In the Bethesda system, cyst fluid only (CFO) cases are a subset of non-diagnostic category.

In this category, maximum cases were of Colloid Goitre (70.86%) similar to the findings of Pattnaik *et al.* (2) and Dhamecha *et al.* (13) and followed by 21.26% cases of lymphocytic thyroiditis. Cases of colloid goitre mostly yielded colloid and microscopically showed abundant colloid with cystic macrophages. Cases of Lymphocytic Thyroiditis showed hurthle cell change, scant colloid and impingement of lymphocytes in the thyroid sheets and clusters, few cases even showed florid lymphocytic thyroiditis resembling lymph node. In all such cases anti-thyroid antibody profile was advised, the most common being anti-thyroglobulin and anti-thyroid peroxidase (TPO).

The three categories AUS, SFN, SFM are often referred to by clinicians as indeterminate thyroid FNAC categories. Although they are associated with well-defined malignancy risks and management guidelines, they have inspired the development of molecular tests to triage patients more effectively and to reduce unnecessary surgery for patients who have a benign nodule.

Category-3, Atypia of undetermined significance (AUS) and Category-5, suspicious for malignancy cases reported in our study were 1.33% respectively comparable with that of Mondal *et al.* (11). Both the cases of AUS on cytology showed increased cellularity, some intact papillary structures but without showing any nuclear features of papillary carcinoma. Some microfollicles were also seen, difficult to differentiate between follicular hyperplastic nodules and follicular adenoma. Both the cases were available for histopathological examination (HPE) and were diagnosed as follicular adenoma. The cytomorphologic interpretation of AUS is subjective (14).

The diagnostic category 4, suspicious for follicular neoplasm identifies the nodule with significant architecture alterations of follicular cells, raising the possibility of a follicular carcinoma and thus triaging the nodule for surgical excision. In our study there were 4 cases (2.67%) diagnosed as SFN based on cytomorphological features of a cellular aspirate comprising of follicular cells with significant cell crowding and showing microfollicular

arrangement. Colloid was scanty or absent. Out of 4 cases, 2 were available for histopathology and came out to be follicular adenoma thus requiring no further therapy.

Histologically follicular carcinoma is distinguished from adenoma by the presence of capsular penetration, vascular invasion or both. Because the defining histologic criteria of invasion cannot be assessed by FNAC, one cannot make a diagnosis of follicular carcinoma from a cytologic specimen. Follicular carcinomas have neoplastic features that are recognizable by cytology, resulting in a suspicious diagnostic category SFN. A significant proportion of cases reported as SFN, prove not to be neoplasms at all but rather adenomatoid nodules in multinodular goitre which is why TBSRTC used SFN rather than follicular neoplasm as the designation for this category.

The category V in TBSRTC is equalled with suspicious for malignancy i.e., suspicious of papillary, medullary and other carcinoma thyroid. In the present study, 2 cases i.e., 1.33% diagnosed as Suspicious for Malignancy (SFM) on FNAC showed increased cellularity with many papillary structures, few cells showing nuclear grooves and inclusions but no true papillary structures were seen. There was difficulty in giving them as truly malignant so we kept them in SFM category and advised follow-up. 1 case of SFM was available for HPE and came out to be papillary carcinoma. Recent studies show that application of molecular based techniques such as RT-PCR for RET/PTC gene and analysis of BRAF mutation are helpful and improve the differentiation of malignant from their benign counterparts among the patients of suspicious category (15,16). A BRAF mutation is found in 44% of the papillary thyroid carcinomas and virtually never in benign thyroid nodules.

Papillary carcinoma is the most common malignancy of thyroid in our study similar to the findings of Laishram *et al.* (17) followed by 1 case each of Medullary and Anaplastic carcinoma thyroid similar to the findings of Singh *et al.* (18). All the cases of papillary carcinoma were seen in young females and microscopically showed the typical features like true papillae with cells showing nuclear inclusions, grooves. One of the cases even showed chewing gum (thick) colloid and psammoma bodies. Medullary carcinoma accounts for 5-10% of all thyroid carcinomas arising from the parafollicular C cells, about 80-90% are sporadic and occur in adults. Rest occurs in children in association with genetic syndromes such as Multiple Endocrine Neoplasia (MEN). Medullary Carcinoma microscopically showed numerous plasma cystoid cells as singly scattered and loose clusters with round nuclei, granular chromatin, inconspicuous nucleoli



and at places pinkish amyloid like material and a diagnosis of Medullary Carcinoma was given which on histopathology came to be same.

Anaplastic carcinoma diagnosis was given on FNAC in a 70 years old male. Cytomorphology showed large cells with marked nuclear pleomorphism along with many multinucleated giant cells. The cells were arranged as large fragments, clusters and individually scattered. HPE of the same was given as undifferentiated carcinoma thyroid (Anaplastic).

The correlation of cytology and histopathology diagnosis is an important quality assurance method as it allows cytopathologists to calculate their false positive and false negative results (19). In our study, the main drawback was not much of the cases were available for HPE after their cytological diagnosis. However, the cases which were available, there was not much discrepancy in cytological and histopathological diagnosis.

Conclusion

Thyroid FNAC is a good screening test to avoid unnecessary thyroidectomies. The technique is easy to perform, cost effective and minimally invasive. FNAC using Bethesda guidelines is useful in improving communication between pathologists and clinicians thus guiding appropriate management, and results in the present study were consistent with the literature.

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Conflicts of Interest

There are no conflicts of interest.

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