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Original Research Article

Cyto–Histopathological Correlation of Various Thyroid Lesions and Evaluation of the Bethesda System for Reporting Thyroid Cytopathology: A 3 Year Retrospective Study

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Abstract

Background: Fine Needle Aspiration Cytology (FNAC) is important for pre-operative and pre-treatment diagnosis of benign and malignant thyroid lesions, thus decreasing the incidence of unwanted surgeries.

Objectives: The present study aims to classify various cytomorphological lesions of the thyroid according to The Bethesda System for Reporting of Thyroid Cytopathology (TBSRTC) and correlate these with histopathology so as to establish the utility of FNAC in the diagnosis of thyroid lesions.

Material & Methods: A retrospective study was conducted in a tertiary care centre to evaluate the diagnostic accuracy of FNAC in lesions of thyroid during a 3 year period. The cytological findings were classified according to the recent TBSRTC and subsequent histopathological correlation was done in all the cases.

Results: Out of total 200 cases studied, benign category (II) was the most common (79.0%) followed up by malignant (VI -11.0%) and follicular neoplasm (IV-9.0%) categories. Cyto-histopathologic correlation of all cases was done. The present study showed 92.85% sensitivity, 100% specificity, 100% positive predictive value, 98.8% negative predictive value and 99% diagnostic accuracy in detecting malignant tumors.

Conclusions: FNAC is a safe, simple, highly accurate, economical and universally accepted modality for evaluation of thyroid lesions especially in developing countries such as India. Use of TBSRTC in reporting thyroid cytopathology has a greater accuracy. There is almost perfect cyto-histopathological concordance and the results are consistent with those available in the literature.

Keywords: Diagnostic Accuracy; FNAC; Histopathology Correlation; Sensitivity; Specificity; Thyroid.

Introduction

The prevalence of thyroid swelling ranges from 4% to 10% in the general adult population and from 0.2% to 1.2% in children. In surgical practice, thyroid lesions are common, observed in 4-7% of the population and affect women more commonly than men [1]. Excising all the thyroid lesions is impracticable and associated with risk [2,3]. As FNAC distinguishes between benign and malignant lesions quite effectively, it is the pre-operative screening method of choice worldwide [4]. In past five or six decades, FNAC of thyroid has been increasingly utilized for investigation of thyroid lesion to know the neoplastic and non-neoplastic lesions.

Simplicity, diagnostic accuracy and most of all cost effectiveness has given FNAC the status of first line diagnostic test in preoperative evaluation of thyroid lesions. However, due to lack of a standardized system of reporting, pathologists have been using different terminologies thus creating confusion among clinicians in the interpretation of reports and further management. In 2007, National Cancer Institute, Bethesda, Maryland, United States published guidelines known as the Bethesda system of reporting thyroid cytopathology (TBSRTC). It is a six category scheme with individual risks of malignancy that influence management paradigms.

The present study was undertaken to find out the incidence of various thyroid lesions in this region of Kerala and to analyse the risk of malignancy in each category obtained by preoperative fine needle aspiration cytology and correlation with histopathological examination and compared with previous studies.

Materials & Methods

This was a retrospective study undertaken in the department of Pathology in a teaching Institution. A prior approval was obtained from the Institutional Ethics committee. Data from medical records of patients who underwent thyroidectomy and preoperative FNAC in this institution were analysed during a period of 3 years [2014 June—2017 June]. For these patients, after taking informed consent, aspiration was performed on thyroid swellings under aseptic precautions. FNAC was performed by the technique described by Orell et al [20]. The procedure was done using 24 gauge needle. Multiple smears were made from the aspirate & fixed in 95% ethanol & stained using the Papanicolau stain . Air dried smears were stained using Giemsa stain. The Bethesda System was used to evaluate the cases. The Bethesda System for Reporting thyroid Cytopathology has six categories:

1. *Non diagnostic ND/unsatisfactory UNS*; Smears were considered as non-diagnostic when a thyroid FNA sample failed to fulfill the recommended criteria for adequacy which are presence of a minimum of six groups of well-visualized follicular cells, with at least ten cells per group, preferably on a single slide, absence of colloid or only blood. Aspirates diagnosed as cystic fluid were recorded as such but considered as non-diagnostic.
2. *Benign BN*; Lesions were classified into this category if they were diagnosed or reported as colloid nodule, multinodular goiter, lymphocytic or granulomatous thyroiditis as well as if the aspirate showed benign follicular cells only.
3. *Atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS)*; Lesions were classified into this category if they were diagnosed or reported as adequate with 'atypical cells/atypical follicular cells' accompanied by a comment stating that neoplasm could not be excluded and that a repeat FNA of the lesion was recommended.
4. *Follicular neoplasm/Suspicious for follicular neoplasm SFN*; Lesions were classified into this category if they were diagnosed or reported as having high follicular cellularity with predominant microfollicle formations, scant colloid. Lesions exhibiting Hurthle cells predominantly and diagnosed as Suspicious for Hurthle cell neoplasm were also included.
5. *Suspicious for malignancy SM;* Lesions were classified into this category if they were diagnosed or reported as being suspicious for papillary, medullary or metastatic carcinoma or lymphoma. Smears in this category were mainly cellular with crowded cell groups exhibiting nuclear and cytoplasmic pleomorphism with some occasional single atypical cells. In the context of suspicious papillary carcinoma rare presence of nuclear enlargement, grooves, overlapping and/or pseudoinclusions along with thick colloid were considered suspicious.
6. *Malignant MGT*; Lesions were classified into this category if they were diagnosed as frankly malignant with type specification.

The postoperative specimens of the same patients were received in 10% formalin in fresh state and allowed to fix for 24 hours. Detailed gross examination was done and bits were given. Paraffin embedded H&E stained sections were obtained and studied under light microscopy. Cyto-histopathological correlation of these cases were also done. All the patients who presented with palpable thyroid lesions and who underwent FNAC with subsequent histopathological examination were included in the study and Patients whose FNAC was not done from this Institution were excluded from this study.

Statistical Package for Social Sciences (SPSS) software was used for statistical analysis. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy (efficacy) were calculated.

Results

The present study included a total number of 200 cases who presented with thyroid lesions. Patients age ranged from 8 to 72years with predominance of female patients with F: M ratio being 7:1. Table 1 shows age and sex wise distribution of thyroid lesions. Majority of the patients were in the age group of 41-60 years followed by 21-40 years. In the present study, the non-neoplastic lesions were more common than neoplastic lesions.

Distribution of FNAC finding according to TBSRTC and the incidence of malignancy in each category is shown in the Table 2. Benign category (II) was the most common (79.0%) followed up by malignant (VI-11.0%) and follicular neoplasm (IV - 9.0%) categories. Non-neoplastic lesions accounted for 160 cases of which colloid goiter was the most common lesion (66.0%) followed by thyroiditis (8.5%). Incidence of malignancy was highest in category VI (100%) followed by category IV (22.2%). All malignant cases detected on cytological study were that of papillary thyroid carcinoma.

Cyto – histopathological correlation of thyroid lesions is shown in Table 3.

Colloid Goitre

Out of 200 cases, 132 cases were diagnosed as colloid goitre by cytology. Histopathological study confirmed the cytodiagnosis in 129 cases. In the remaining 3 cases, 2 cases turned out to be colloid goitre with micropapillary carcinoma, while the other case showed thyroiditis.

Follicular Neoplasm

Out of 200 cases, 18 cases were diagnosed as follicular neoplasm by cytology. 6 cases were confirmed by histopathology as follicular adenoma and 2 cases as follicular carcinoma. The rest 4 cases turned out to be adenomatous goitre, 3 cases as colloid goiter, 2 cases as follicular variant of papillary carcinoma and 1 case as thyroiditis. Gross picture of follicular adenoma is shown in the figure 1a, whereas figure 1b and 1c show the cytology of follicular neoplasm and histopathological section of follicular adenoma respectively.

Thyroiditis

Out of 200 cases, 17 cases were diagnosed as thyroiditis by cytology. The histopathological study confirmed 16 cases and the remaining 1 case turned out to be adenomatous goitre.

Papillary Carcinoma

Out of 200cases, 22 cases were diagnosed as papillary carcinoma by cytology and all the cases were confirmed by histopathology. Figure 2 shows the gross and microscopy of papillary thyroid carcinoma.

Of the 200 cases, 174 cases were diagnosed as benign and only 26 cases turned out to be malignant by FNAC, where as 172 cases were diagnosed as benign and 28 cases turned out to be malignant by histopathology resulting in 2 false negative cases (Table 4). The present study showed 92.85% sensitivity, 100% specificity, 100% positive predictive value, 98.8% negative predictive value and 99% diagnostic accuracy in detecting malignant tumors.

Table 1: Age and sex distribution of thyroid lesions

Sex	Age Distribution (years)				
	<20	21 -- 40	41 -- 60	61 -- 80	Total
Male	1	7	14	3	25
Female	3	73	88	11	175
Total	4	80	102	14	200

Table 2: Cytological diagnosis of thyroid lesions according to Bethesda system

Bethesda	Frequency	Percent	Incidence of malignancy
I (Nondiagnostic)	2	1.00%	0.00%
II (Benign)	158	79.00%	1.27%
III (Atypical follicular lesion of undetermined significance)	0	0%	0.00%
IV (Follicular neoplasm)	18	9.00%	22.2%
V (Suspicious for malignancy)	0	0%	0.00%
VI (Malignant)	22	11.00%	100.0%
Total	**200**	100.00%	

Table 3: Cytohistopathological correlation of thyroid lesions

Cytological Diagnosis	Histopathological Diagnosis							
	Thyroglossal cyst	Colloid goitre	Thyroiditis	Adenomatous goitre	Follicular adenoma	Follicular carcinoma	Papillary carcinoma	Total
Nondiagnostic	0	2	0	0	0	0	0	2
Thyroglossal cyst	3	0	0	0	0	0	0	3
Colloid goitre	0	129	1	0	0	0	2	132
Adenomatous goitre	0	1	0	4	1	0	0	6
Thyroiditis	0	0	16	1	0	0	0	17
Follicular neoplasm	0	3	1	4	6	2	2	18
Papillary carcinoma	0	0	0	0	0	0	22	22
Total	3	135	18	9	7	2	26	200

Table 4: Cytohistopathological correlation of thyroid lesions

Cytological Diagnosis	Histopathology Diagnosis		
	Benign	Malignant	Total
Benign	172	2	174
Malignant	0	26	26
Total	172	28	200

Table 5: Comparison of results of present study with previous studies in identifying thyroid malignancies

Studies	Year	Sensitivity	Specificity	Accuracy
Gupta et al.(6)	2010	80.00	86.60	84.00
Pinky pandey et al.(22)	2012	57.14	90.00	80.28
Parikh et al.(23)	2012	71.43	100	90.24
Ranjan et al.(9)	2014	82.14	86.80	83.60
Gamit et al.(24)	2015	92.85	98.48	97.5
Aramani et al.(25)	2015	96.36	100	96.66
Present study	2017	92.85	100	99.00

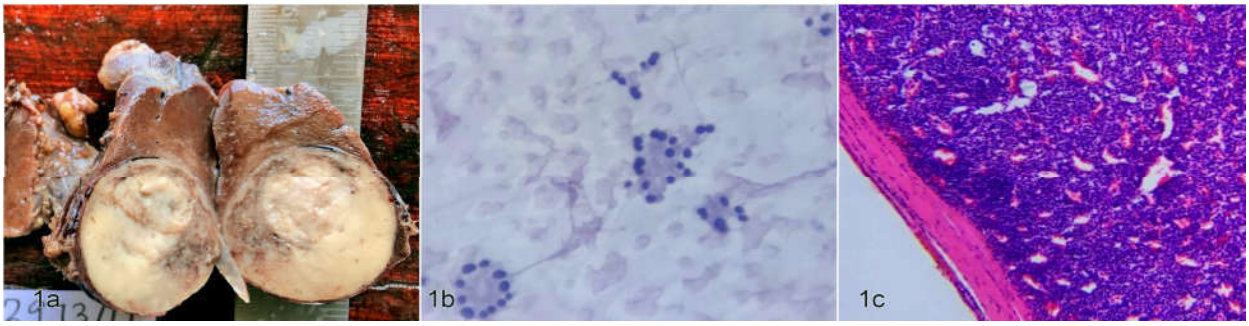

Fig. 1: 1a: Gross picture of follicular Adenoma, **1b:** Photomicrograph of cytology of follicular neoplasm (Bethesda category IV) (PAP stain, 40x), **1c.** Photomicrograph of histopathological section of follicular adenoma (H&E stain, 40x)

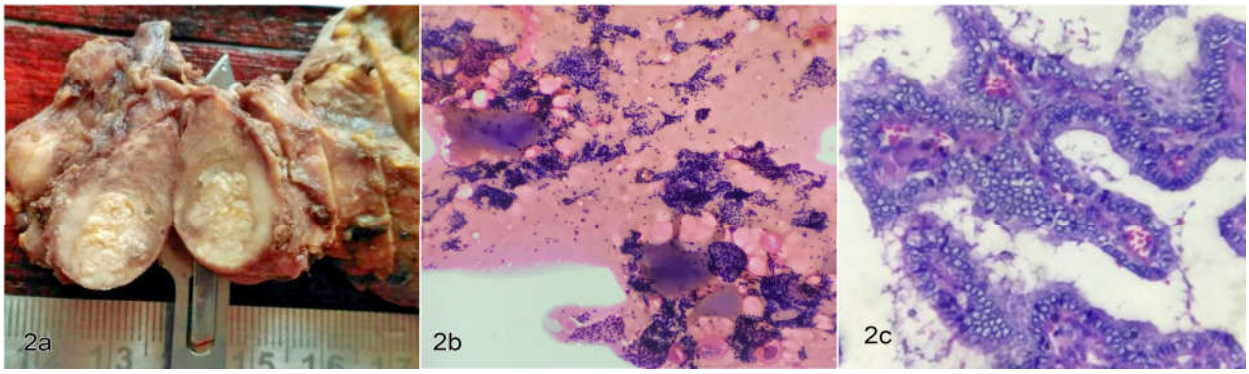

Fig. 2: 2a: Gross picture of Papillary Thyroid Carcinoma, **2b:** Photomicrograph of cytology of Papillary carcinoma (PAP stain, 40x), **2c:** Photomicrograph of histopathological section of Papillary carcinoma (H&E stain, 40x)

Discussion

Thyroid FNAC was initially started by Martin and Ellis in 1930. The terminology used for reporting thyroid FNAC has shown significant inter-laboratory variations, creating confusions and also interfering with the data exchange among different centres. Keeping this in view in 2007 TBSRTC was evolved with the aim of forming a uniformity in the reporting of FNAC findings of thyroid that would facilitate effective discussion among cytopathologists and clinicians; facilitate correlation between cytopathology and histopathology, epidemiological studies, molecular genetics, and, diagnostic interpretation of thyroid diseases in particular neoplasia. It also ensured that the data between various laboratories and institutions could be shared without any specific interpretive mistakes [5].

A total of 200 cases of thyroid lesions who underwent FNAC with subsequent histopathological examination were included in the study and all the lesions were analysed

with their history, FNAC findings and histopathology. Palpable thyroid nodules are more common in females with a F: M ratio of 4.2:1 [6-8]. In the present study also there was a female predominance with F: M ratio of 7:1. It was similar to the studies done by Ranjan et al [9] and Tilak et al [10]. Age of the patients ranged from 8-72 years and majority of the patients were in 41- 60 years followed by 21-40 years. It is in discordance with the study done by Kumar et al [11] where majority of the patients were in 21 – 40 yrs.

In our study the nondiagnostic category constituted 1% (2 cases). Few authors suggest that the rate of non-diagnostic tests should be kept below 10% [12]. The risk of malignancy reported in the ND/UNS (not including cyst fluid only) category ranges from 1% to 5.5% [13-16]. A repeat aspiration under high ultrasound guidance is recommended in such cases. However, some nodules remain persistently ND/UNS even on repeat aspirations and should be subjected to surgical excision. Non-diagnostic or insufficient samples are common in nodules that are calcified, sclerotic or in those that have undergone major cystic degeneration [9]. In our study that 2 cases were diagnosed as colloid goitre with marked cystic degeneration on histopathological examination.

As in the available literatures, the benign category represented the majority of cases. In our study benign category constituted 79% (158 cases) of cases. This is in accordance to the previous other studies [9]. The lesions included in the benign category were thyroglossal cyst, colloid goitre, adenomatous goitre and thyroditis. As in other studies, the commonest benign lesions were colloid goiter (66%) followed by thyroiditis (8.5%) [17,18]. 2 cases were diagnosed as colloid goitre with micropapillary carcinoma by histopathology and resulted in 2 false negative cases. Gagneten stressed the importance of doing multiple aspirations in a thyroid swelling in order to obtain representative material from different areas since the thyroid can be affected by more than one disease process [19]. Thus we can avoid false negative cases by doing repeat aspiration or by doing USG guided FNAC.

The category of Follicular neoplasm forms a gray zone with various differentials such as follicular carcinoma, follicular variant of papillary carcinoma, follicular adenoma and adenomatoid nodule [9]. In the present study, out of 200 cases, 18 cases were diagnosed as follicular neoplasm by cytology. 6 cases were diagnosed by histopathology as follicular adenoma, 4 cases as adenomatous goitre, 3cases as colloid goiter, 2 cases as follicular carcinoma, 2 cases as follicular variant of papillary carcinoma and 1 case as thyroiditis. 3 cases of colloid goitre were misdiagnosed as follicular neoplasm in FNAC, it is a known fact that the cytological criteria cannot reliably differentiate between the two because of the overlap. Smears from micro follicular areas in a nodular goitre may show a repetitive pattern of micro follicles or rosettes similar to the follicular neoplasm, and if only such a focus is aspirated and sampled, the differentiation from follicular neoplasm is impossible [20]. In the present study similar type of microfollicular areas were sampled and lead to the erroneous diagnosis of follicular neoplasm.

The malignant category constituted 11% (22 cases) of cases and all the cases were papillary thyroid carcinoma which is congruent to other studies (17,21). In our study no cases were diagnosed as category 3 (AUS) or category 5 (suspicious of malignancy).

In our study the incidence of malignancy for benign category was 1.27%, for follicular neoplasm 22.2% and for malignant category 100%. This was comparable with the TBSRTC guidelines where the risk of malignancy for benign category, follicular neoplasm and for malignant category where 0 – 3%, 15-30% and 97-99% respectively [5].

Statistical analysis in our study revealed a sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 92.85%, 100%, 100%, 98.8% and 99% respectively. This study is comparable with the other studies as shown in the table 5.

Conclusions

FNAC exhibits an adequate diagnostic correlation with the final histopathological examination and enables a comparison of results between different institutions. Our results are consistent with those available in the literature. If the cytology report is malignant, surgery is the recommended procedure; for suspicious lesions, repeat aspiration is required and for benign lesions no further immediate diagnostic studies are required. FNAC is an invaluable tool in the management of thyroid lesions with a high degree of accuracy.

It is safe, simple, cost-effective procedure with absence of major complications and can be performed on out- patients with wide patient compliance. FNAC provides a more rapid and accurate diagnosis of thyroid lesions than any other combination of clinical laboratory tests.

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