Thyroid Cytopathology Reporting According to Bethesda System with Histopathological Correlation

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Abstract:

Objective: The objective of present study was to classify and report the thyroid lesion by using the Bethesda system in reporting thyroid FNAs and To correlate cytological with histological finding and to assess the value of TBSRTC in the distribution of diagnostic categories and to evaluate the specificity of system.

Material and method: This study was prospective cross sectional study conducted for one year duration from Feb 2020 to March 2021 at Pt. JNM Memorial Medical College Raipur. A total number of 100 patients belonging to age group of 11- 80 years were include in the study. All fnac are classified according to TBSRTC and histopatholgical correlation was done with all available sample.

Result: A total of 100 patients included in this study. Age ranged from 11- 80 year. Most common age group affected was 31-40 years. Mean age of patient was 38 years. Male female ratio was 1: 4. Distribution of cases according to Bethesda category was as follows: Cat I 18% Cat II 57%, Cat III 02%, Cat IV 08%, Cat V 07%, Cat VI 08%. Histopathological specimen was available in 60 sample. Histopathological diagnosis was found consistent with cytological diagnosis in 66.66% cases. Sensitivity and specificity for diagnosis of thyroid malignancy were 76.9% and 89.4% respectively. Overall accuracy was 86.27%.

Conclusion: The Bethesda system of reporting thyroid cytopathology is a valuable classification of thyroid aspirates. It improves communication between pathologist and clinicians and surgeons. It help them to know prognosis and risk of malignancy in each category, and provides guidelines in patient management.

Keywords: Bethesda system, thyroid cytopathology, TBSRTC.

Introduction

Fine needle aspiration cytology is well established outpatient procedure used in the primary diagnosis of palpable thyroid swelling. Fine needle aspiration cytology (FNAC) is first line investigation part from other investigations like ultrasonography (USG), thyroid function test, antibody levels for the primary evaluation of the patients. [1] FNAC is an easy, cost effective test for cancer diagnosis, and its use markedly decreased the number of unnecessary thyroid surgeries.

Prevalence of palpable thyroid nodule in non-iodine deficient area is about 4-7% in general adult population and 0.2 to 1.5 % in children [2,3]. Now a days due to common use of USG in clinical practice the incidence of thyroid nodule has risen to 14- 50% [3,4,5]. Benign lesions are more common in thyroid and less than 5% are actually malignant [3,5] .

Both benign and malignant lesions of thyroid commonly present with a nodule. Since most of the thyroid nodules are benign it is essential to identify patients who are likely to be benefited from surgery and thus avoid essential diagnostic surgery in all cases.

In the year 2007, the National Cancer Institute (NCI), Bethesda, Maryland, United States, organized the NCI Thyroid Fine Needle Aspiration State-of-the-Science Conference, and an initiative was undertaken to publish an atlas and guidelines using a standardized nomenclature for the interpretation of thyroid fine needle aspirates (FNAs), known as the Bethesda system for reporting thyroid cytopathology.

The atlas describes six diagnostic categories of lesions: Non-diagnostic/unsatisfactory, benign, atypical follicular lesion of undetermined significance (AFLUS), "suspicious" for follicular neoplasm (SFN), suspicious for malignancy (SM), and malignant. The six diagnostic categories of the Bethesda system have individual implied risks of malignancy that influence management paradigms. [6]

Material and Methods

A prospective study of all FNA's of thyroid swelling were conducted between 2016-2017 and classified according to the TBSRTC 6-tier diagnostic categories and tissue sections were obtained subsequently wherever histopathological specimen were available. A concise clinical history, examination, and details of relevant investigations were also included. These were helpful in reaching a probable clinical diagnosis as well as in cytohistological evaluation and formulations of the pathological diagnosis. The data included 100 cases of thyroid FNAC and 60cases of follow-up histopathological specimens. all cases had been reported using TBSRTC. The smears were prepared using conventional methods and alcohol fixed smear were stained with Papanicolaou stains/Haematoxylin and Eosin and air dried smears were stained with MGG (May Grunwald and Giemsa) stain. Histopathological specimen was processed as per standard methods. Total 100 cases were included in the study.

Result

100 Cases were included in the studied**.** Most common age group affected was 31-40 years. Mean age of patient was 38 years. 79% patients were female and 21 % patients were male. Male female ratio was 1: 4. The Distribution of cases according to Bethesda category was as follows: Cat I 18%, Cat II 57%, Cat III 02%, Cat IV 08%, Cat V 07%, Cat VI 08%.

Out of 100 cases of thyroid swelling diagnosed on FNAC, histopathological specimen was available for 60 cases. Cytological diagnosis was compared with histopathological diagnosis. Histopathological diagnosis was found consistent with cytological diagnosis in 66.66% cases. Sensitivity and specificity for diagnosis of thyroid malignancy were 76.9% and 89.4% respectively. Overall accuracy was 86.27%.

Discussion

History of fine needle aspiration cytology (FNAC) dates back to middle of nineteenth century. Kun and Lebert (1846) used to diagnose cancers by employing this technique. [7,8] Fine Needle Aspiration Cytology was first used as a method for diagnosing thyroid gland diseases by Soderstrom and Franzen in the 1950s and 1960s. [9,11] The National Cancer Institute (NCI) hosted the "NCI Thyroid Fine Needle Aspiration State of the Science Conference" on October 22 and 23 in 2007 in Bethesda. In January 2010 they implemented a uniform reporting system (6 tier Bethesda System for Reporting Thyroid Cytopathology - TBSRTC) for thyroid FNA. This facilitated effective communication among cytopathologists and the clinicians conveying specific risks of malignancy, which offers guidance for patient management, helping in reduction of the surgeries in benign cases and increasing the number of malignancies in resection. [6]

This system divided six diagnostic categories of thyroid lesion –

The Bethesda System for Reporting Thyroid Cytopathology: Implied Risk of Malignancy and Recommended Clinical Management [12]

Table: 1

Diagnostic Category	Risk of Malignancy (%)	Usual Management†
Nondiagnostic or Unsatisfactory	1-4	Repeat FNA with ultrasound guidance
Benign	0-3	Clinical follow-up
Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance	~5-15‡	Repeat FNA
Follicular Neoplasm or Suspicious for a Follicular Neoplasm	15-30	Surgical lobectomy
Suspicious for Malignancy	60-75	Near-total thyroidectomy or surgical lobectomy§
Malignant	97-99	Near-total thyroidectomy§

FNA, fine-needle aspiration.

† Actual management may depend on other factors (eg, clinical, sonographic) besides the FNA interpretation.

‡ Estimate extrapolated from histopathologic data from patients with "repeated atypicals."

§ In the case of "Suspicious for metastatic tumor" or a "Malignant" interpretation indicating metastatic tumor rather than a primary thyroid malignancy, surgery may not be indicated.

Table 2: Distribution of FNAC of thyroid lesions results according to subcategory of Bethesda System

Category	Subcategory	Number of cases	Total no. of cases under each category
Category I	Vertually Acellular specimen	07	18 (18%)
	Cystic fluid only	02	
	Others (obscuring blood, artefact etc.)	09	
Category II	Colloid goitre	41	57 (57%)
	Lymhocytic thyroiditis	10	
	Granulomatous thyroiditis	02	
	Others	04	
Category III	Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance	01	01 (01%)
Category IV	Follicular neoplasm/Suspicious for Follicular Neoplasm	08	08 (08%)
Category V	Suspicious for malignancy	07	07 (07%)
Category VI	Medullary carcinoma	02	09 (08%)
	Papillary carcinoma	07	
Total		100	100%

Table 3: Comparison of FNAC diagnosis by various authors according to Bethesda classification:

FNAC Diagnosis	Year	CAT I	CAT II	CAT III	CAT IV	CAT V	CAT VI	Total No of Cases
Yassa et al [22]	2007	7%	66%	4%	9%	9%	5%	2587
Jo et al [113]	2010	18.6%	59.0%	3.4%	9.7%	2.3%	7%	3080
Wu et al [21]	2011	20.1%	39%	27.2%	8.4%	2.6%	2.7%	1382
Mondal et al [15]	2013	1.2%	87.5%	01%	4.2%	1.4%	4.7%	1020
Bhagat et al [23]	2014	5.63%	87.5%	0%	3.12%	0.63%	3.12%	160
Muratli et al [17]	2014	10.8%	59.5%	8.7%	0.6%	2.8%	17.6%	1333
Agrawal et al [10]	2015	2.49%	87.90%	3.91%	2.49%	1.78%	1.42%	281
Gupta V et al [20]	2015	11%	78%	02%	3%	0%	6%	300
Kapila et al [19]	2015	4.8%	30.5%	15.8%	4.5%	21.4%	23%	374
Lohiya et al [18]	2016	4%	88%	2%	1.6%	0.8%	3.6%	250
Present study	**2017**	**18%**	**57%**	**01%**	**8%**	**07%**	**9%**	**100**

In the present study peak age group was 31-40 years constituting 28% of all patients with age range of 11-80 years. Mean age of presentation of thyroid lesion was 38.24 years, which is similar to study done by Garg et al (2015) [9], Agrawal et al (2015) [10] i.e. 38.50 years and 38.24 years respectively. Arul et al (2015) [11] also reported mean age of thyroid lesion as 38.22 years with age range of 16-80 ye In the present study, out of 100 patients 79 % were female and 21% were male. Male female ratio was 1: 3.8, which is quite comparable with the study done by Agrawal et al (2015) [10]. Maximum mean age of 49 years was reported by Laishram et al (2017) [12].

Category I (Nondiagnostic / Inadequate) - in the present study the rate of non-diagnostic result was 18 % which is similar to study done by Jo et al (2010) [13]. Non diagnostic or insufficient samples are common in nodule that is calcified, sclerotic or in those that have undergone major cystic degeneration [10]. Nondiagnostic specimens are a major limitation of thyroid fine needle aspiration

with most studies reporting rates between 10% and 20% [14].

In present study, the percentage was high probably due to the fact that, if the thyroid nodule was palpable then FNAC was done blindly without USG guidance. Percentage of Nondiagnostic cases can be reduced by FNAC under USG guidance. Mondal et al (2013) [15] reported minimum 1.2 % cases under Nondiagnostic category because they performed FNA under USG guidance.

Category II (Benign) – In the present study most of the lesion (57%) were found to be benign. Among these most of the cases were of colloid goitre followed by thyroiditis. Present study correlate well with the study done by Sharma et al (2017) [16], Muratli et al (2014) [17] and Jo et al (2010)15 as they also reported 74%, 59.5%, and 59% benign cases respectively. In recent studies benign category had a range of 30.5% to 88% [29,33]. Lohiya et al (2017) [18] also reported benign category (88%) to be the most common category. Minimum 30.5% cases were reported by Kapila et

al (2015) [19]. TBSRTC recommended management for this category is clinical follow up.

Category III (Atypia of undetermined significance /Follicular lesion of undetermind significance) - in the present study only 1% case was diagnosed as atypia of undetermined significance. Present study was quite comparable with study done by Gupta V et al (2015) [24] and Lohiya et al (2017) [18]. TBSRTC suggest that the frequency of AUS interpretation should be in the range of 7% of all thyroid FNA interpretations. Maximum 27% cases were reported in AUS category by Wu et al (2011) [21]. Various literatures shows the range of AUS/FLUS between 1% to 27.7% 17, 20. Out of 2 cases only 1 case was available for histopathological examination which was diagnosed as follicular variant of papillary carcinoma. TBSRTC recommended management for this category is repeat FNA.

Category IV (Follicular neoplasm / Suspicious for Follicular Neoplasm) –

In the present study only 8% cases were diagnosed as follicular neoplasm. Wu et al (2011) [21] reported similar finding in his study .various literature shows range of category IV between 0.6 % to 9.7%. Minimum 0.6% cases were reported by Muratli et al (2014) [17]. Whereas maximum 9.7% cases were reported by Jo et a (2010) [13]. TBSRTC recommends lobectomy for this category.

Category V (Suspicious for malignant) – in the present study only 7% cases were reported under category V which is almost similar to study done by Yassa et al (2007) [22]. Maximum 21 % cases were reported by Kapila et al (2015) [19]. Minimum 0.63% cases were reported by Bhagat et al (2014) [23].TBSRTC recommended management for this category is near total thyroidectomy or surgical lobectomy.

Category VI (Malignant) – the malignant category is used whenever the cytomorphologic features are indicative of malignancy. In present study only 9% cases were reported under this category which is quite comparable with study done by Jo et al (2010) [13]. Out of 9 cases 7 cases were of papillary carcinoma and rest 2 cases were of medullary carcinoma. A malignant thyroid FNAC is expected to account for 4-8% of all thyroid FNACs [18]. The risk of malignancy is 97-99%. In this category TBSRTC recommended management is total thyroidectomy.

The correlation of cytological and histopathological diagnoses is an important quality assurance method, as it allows cytopathologists to calculate their false positive and false negative results .The false negative rate (FNR) is defined as the percentage of cases with benign cytology but proven to be malignant after histopathological examination. It may occur because of sampling error or misinterpretation of cytology and are of great concern because they indicate the potential to miss a malignant lesion. Unfortunately; it is difficult to calculate the true frequency of false negative results as only a small percentage of patients with benign cytological findings undergo surgery. The false positive rate (FPR) is defined as percentage of cases with a malignant FNA proven to be benign on histological examination. [25]

In present study cytohistological concordance rate was achieved in 36 (70.5%) cases whereas 17 (29.5%) cases were discordant on histopathology. One cases of cytologically diagnosed colloid goitre were turned out to be follicular adenoma. It may be due to small lesion in thyroid with multiple nodules leading to sampling error, misinterpretation as hyperplastic nodule. Cytologically it is difficult to distinguish nodular goitre and colloid rich follicular adenoma. Cytological features like increased cellularity with repetitive uniform cell patterns, uniformly enlarged nuclei with nuclear crowding and overlapping, syncytial clusters, microfollicular structures, scanty or no colloid may be helpful in distinguishing follicular adenomas from nodular goiters, although none of them is conclusive. [26] One case of follicular neoplasm is histologically turned out to be colloid goitre .Cause of discordance may be aspiration from hypercellular area which lead to misinterpretation. Papillary carcinoma was misdiagnosed on cytology as goitre due to faulty sampling from cystic area rather than from the tumour itself, resulting in the paucity of neoplastic follicular cells. Cystic changes in the thyroid lesions have always been a common diagnostic pitfall in cytology. Hence, it is recommended to prepare 4-6 smears from different areas of the lesion to reduce sampling error as well as to employ ultrasound guided FNAC in cystic and heterogenous lesions to increase overall accuracy. One case of cytologically diagnosed papillary carcinoma was diagnosed as lymphocytic thyroiditis on histopathology .it may be explained on the basis of overemphasis on papillary architecture and nuclear inclusion. The minimal criteria for cytodiagnosis of papillary carcinoma include, a syncytial-type tissue fragment regardless of architectural pattern, typical nuclear features i.e. pale enlarged nuclei with fine dusty, powdery chromatin; chromatin bar or ridge; single or multiple micro-and/or macro nucleoli; and intranuclear cytoplasmic inclusion. [27]

The follicular variant of papillary carcinoma is a pitfall in thyroid FNAC. Cytologically, it presents with hypercellularity with a prominent follicular pattern but no obvious papillae. Syncytial follicular cells, nuclear grooves, intranuclear pseudoinclusion and chewing gum colloid have been reported to be occasionally present in variable proportions.

However, none of these cytological pictures are specific, and may present in adenomatous goiters, follicular adenomas and follicular carcinomas at varying frequencies. [28] Leung et al (1993) [29] revealed that the true nature of the histological variants of the papillary carcinoma cannot be predicted from the appearances of the FNAC. Multiple aspirations can be done 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.

In our study false negative rate was 23% and false positive rate was 10%. False negative result can occur due to sampling error or misinterpretation of cytology. Since only a small percentage (approximately 10%) of patients with benign cytologic findings undergo surgery, it is difficult to state the true frequency of false negative results. [30] Clinical sensitivity and specificity are the most common predictive parameter used in evaluation of diagnostic tests. The clinical sensitivity of thyroid fine needle aspiration would indicate the frequency of test results that were positive for patient with thyroid disease and clinical specificity would indicate the frequency of test results that were negative for patient without thyroid disease.In present study sensitiviy and specificity was reported as 83.3% and 89.7% respectively which is quite comparable with study done by Bhatta S et al (2012) [31] and Thotakura et al (2015) [32]. Highest sensitivity (97%) was reported by Bongiovanni et al (2012) [33] and highest specificity (97.4%) was reported by Arul et al (2015) [11]. Sensitivity and specificity of FNAC ranges from 76.9%-97% and 50.7%-100% respectively. Thus FNAC is found to be very effective in differentiating malignant lesion from benign lesion.

Conclusion

FNAC is an important tool in the management of thyroid lesion. It is safe, simple, cost effective procedure without major complication. It can be performed as outpatient procedure with good patient compliance. It helps in differentiating lesions that require surgery from those that can be managed otherwise. The Bethesda system of reporting thyroid cytopathology is a valuable classification of thyroid aspirates. It improves communication between pathologist and clinicians and surgeons. It help them to know prognosis and risk of malignancy in each category, and provides guidelines in patient management.

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