Cytomorphological Study of Thyroid Nodule and Categorization According to The Bethesda System and Its Histopathological Correlation

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ABSTRACT

Background: Among an endocrine disorder, thyroid disorders are most commonly encountered disorder in routine clinical practice. Clinically it is quite difficult to evaluate thyroid lesion and reach clinical diagnosis. FNAC (Fine needle aspiration cytology) of thyroid is commonly performed and most effective tool for diagnosis and management of patient with thyroid nodule. Present study was conducted in department of pathology, government medical college, Surat. Our main aims and objectives are to report thyroid cytology smears by TBSRTC in to various diagnostic categories and to correlate these with histopathological findings.

Material and Method: In the present study FNAC was performed on total 250 cases that were presented with thyroid swelling. These cases categorized according to TBSRTC and cytological diagnosis was correlated histopathologically in total 21 cases. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated.

Results: FNAC was carried out in 250 cases, diagnostic categories includes 5.20% non-diagnostic, 87.60% benign, 2.80% Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance, 2.40% follicular neoplasm or suspicious for follicular neoplasm, 1.60% suspicious for malignancy and 0.40% malignant lesions. Subsequent histopathological correlation was possible in 21 cases. In present study accuracy, specificity, positive predictive value and negative predictive value of FNAC in diagnosis of thyroid were 95%, 85.71%, 100%, 100% and 92.85% respectively.

Conclusion: Standardized categorical Bethesda systems for reporting thyroid FNAC can make results easier to understand and interpret for clinicians and give clear indications for therapeutic action.

Keywords: Bethesda System, Fine Needle Aspiration Cytology And Histopathology

Introduction

Among an endocrine disorder, thyroid disorders are most commonly encountered disorder in clinical practice. Clinically it is difficult to evaluate thyroid lesion and reach clinical diagnosis. FNAC (Fine needle aspiration cytology) of thyroid is most commonly performed and most effective tool for diagnosis and management of patient with thyroid nodule. Fine-needle aspiration cytology (FNAC) helps in triaging the patients who require surgery for a neoplastic disorder from those who have functional or inflammatory abnormality and who can be followed clinically or treated medically. FNAC is now a first-line, simple, cost effective, minimal invasive and quick screening test as well as the diagnostic tool. It has a high sensitivity and specificity for identifying thyroid malignancies with an average range of 83% and 92% respectively.

In the past, cytomorphological reporting of thyroid aspirate ranged from histology-equivalent categories to categories like equivocal, inconclusive, indeterminant, atypical, suspicious, uncertain, malignancy suspicious, possibly neoplastic, possibly malignant and probably malignant to report thyroid aspirates that fell between benign and malignant diagnostic categories. 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. To address the variability in terminology and other issues related to thyroid FNA, the National Cancer Institute proposed “Bethesda System for reporting of thyroid cytopathology” (TBSRTC). This system represents an important step toward standardization and reproducibility of Thyroid FNAC reporting its clinical significance and predictive value of thyroid FNA.

There is a vivid description of the six diagnostic categories of thyroid lesions. They are non-diagnostic or unsatisfactory, benign, atypia of undetermined significance/ follicular lesion of undetermined significance, follicular neoplasm/ “suspicious” for follicular neoplasm, suspicious for malignancy and malignant. Our aims and objectives are to report thyroid cytology smears by TBSRTC in to various diagnostic categories and to correlate these with histopathological findings whenever possible.

Material and Method

Our study was undertaken to evaluate cytomorphology in outdoor and indoor patients presenting with palpable
thyroid lesions and compared them histopathologically wherever specimen was received after surgery to determine its diagnostic accuracy. All the patients referred for FNAC of thyroid lesions were studied prospectively for a period from January 2017 to July 2018 in the Department of Pathology, Government Medical college, Surat and patients having anterior neck swelling other than thyroid were excluded.

All the patients were clinically examined in sitting upright position and a careful palpation of the thyroid was done for precise location to do aspiration. Details of the procedure were explained to the patients and written consent of patient was taken. Patient was asked to lie down in supine position with pillow under shoulder for hyperextension and lesion was made more prominent by this method. After instructing the patient to refrain from swallowing, under aseptic precautions 23 gauge needle attached with syringe was inserted into the lesion and to and fro movement quickly and gently at different angle and points of entry was done. Material was deposited on several clean and labelled glass slides. After aspiration few slides were fixed in 95% ethyl alcohol, stained by routine H and E method and Pap method, other were air dried and stained with MGG stain. All the slides were examined thoroughly. The reporting was done according to The Bethesda System for Reporting Thyroid Cytology (TBSRTC).

During the period of this study from January 2017 to July 2018, total 250 indoor and outdoor FNA was done from thyroid, among them 21 specimens of thyroid were received after surgery and subjected to histopathological study.

All the specimens were fixed in 10% formalin. Detailed gross examination was done and sections were given from selected representative area for routine paraffin processing. Slides were stained by H and E stain.

Correlation of cytological and histopathological findings was performed. Sensitivity, specificity, accuracy, positive predictive value and negative predictive value were calculated for thyroid lesions by using methodology of Galen and Gambino. [6]

**Results**

FNAC was performed on total 250 patients who were presented with thyroid nodule or swelling. In our study age of the patients ranged from 7-75 years. Most of the patients presented in age group of 21 to 30 years (Table 1). In our study 22(8.80%) cases were of males and 228(91.20%) cases were of females. Male to female ratio was 1:10.3 in our study.

In present study, out of total 250 cases of thyroid lesions, maximum cases, 219(87.60%) were of benign lesion category II, followed by 13(5.20%) cases which were nondiagnostic or unsatisfactory category I. In present study only one case was diagnosed as malignant category VI (Table 2).

In histopathological correlation total 13 cases of benign thyroid lesion diagnosed as benign lesion histopathologically (True negative), 6 cases of malignant thyroid lesion confirmed histopathologically (True Positive) and one case of cystic colloid goiter diagnosed as adenomatoid goiter with micropapillary carcinoma histopathologically (False Negative). Sensitivity, specificity, accuracy, positive predictive value and negative predictive value were calculated for thyroid gland lesions by using methodology of Galen and Gambino (Table 3).[6]

In present study overall accuracy, sensitivity, specificity, positive predictive value and negative predictive value of FNAC in diagnosis of benign and malignant lesions of thyroid were 95%, 85.71%, 100%, 100% and 92.85% respectively.

| Age (years) | 1-10 | 11-20 | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | 71-80 | Total |
|-------------|------|-------|-------|-------|-------|-------|-------|-------|-------|
| I           | 0    | 1     | 7     | 1     | 4     | 0     | 0     | 0     | 13    |
| II          | 2    | 24    | 68    | 51    | 38    | 26    | 5     | 5     | 219   |
| III         | 0    | 0     | 2     | 1     | 1     | 2     | 1     | 0     | 7     |
| IV          | 0    | 0     | 0     | 0     | 1     | 4     | 1     | 0     | 6     |
| V           | 0    | 3     | 1     | 0     | 0     | 0     | 0     | 0     | 4     |
| VI          | 0    | 0     | 0     | 0     | 1     | 0     | 0     | 0     | 1     |
| **Total**   | 2    | 28    | 78    | 53    | 45    | 32    | 7     | 5     | 250   |
| **Percentage** | 0.80% | 11.20% | 31.20% | 21.20% | 18% | 12.80% | 2.80% | 2% | 100% |
Table 2: Cytodiagnosis of thyroid gland lesions according to the Bethesda categories.

| Bethesda Diagnostic categories                                                        | No. of cases | Percentage |
|---------------------------------------------------------------------------------------|--------------|------------|
| I- Nondiagnostic or Unsatisfactory                                                    | 13           | 5.20%      |
| II - Benign Thyroid Lesion                                                            | 219          | 87.60%     |
| III- Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance | 7            | 2.80%      |
| IV- Follicular Neoplasm or Suspicious for a Follicular Neoplasm, specify if Hurthle cell(oncocytic) type | 6            | 2.40%      |
| V Suspicious for Malignancy                                                           | 4            | 1.60%      |
| VI Malignant                                                                          | 1            | 0.40%      |
| **Total**                                                                             | **250**      | **100.00%**|

Table 3: Histopathological diagnosis and Correlation between cytodiagnosis and histodiagnosis.

| Cytological diagnosis         | Histological diagnosis                  | No. Of cases(21) | Remarks |
|-------------------------------|-----------------------------------------|------------------|---------|
| Benign Follicular Nodule      | Colloid goiter                          | 3                | True Negative=13 |
| Benign Follicular Nodule      | Adenomatoid goiter                      | 1                |         |
| Colloid goiter                | Colloid goiter                          | 4                |         |
| Colloid goiter                | Adenomatoid goiter                      | 2                |         |
| Cystic colloid goiter         | Colloid goiter with cystic changes      | 1                |         |
| Hashimoto’s thyroiditis       | Hashimoto’s thyroiditis                 | 1                |         |
| Hyperplastic nodule           | Adenomatoid goiter                      | 1                |         |
| Suspicious for malignancy Medullary Carcinoma | Medullary Thyroid Carcinoma | 2 | True Positive=6 |
| Suspicious for malignancy Papillary Carcinoma. | Papillary carcinoma of thyroid | 2 |         |
| Follicular Neoplasm           | Poorly differentiated carcinoma          | 1                |         |
| Suspicious for a Follicular Neoplasm | Follicular variant of Papillary carcinoma of thyroid | 1 |         |
| Cystic colloid goiter         | Adenomatoid goiter with micropapillary carcinoma | 1 | False Negative=1 |
| Atypia of Undetermined Significance | Adenomatoid goiter with degenerative changes | 1 |         |

Discussion

FNAC is a well-established outpatient procedure used in the primary diagnosis of any swelling. FNAC of the thyroid is the one of main preoperative investigation of thyroid lesions. Due to superficial location of thyroid gland, it is very easy to do FNAC[9,12]

In the present study, 250 indoor and outdoor patients were presented with thyroid swelling in government medical college, Surat during period from January 2017 to July 2018. Fine needle aspiration was done from all these thyroid lesions. In present study, patient variably presented with euthyroid state, hypothyroidism and hyperthyroidism. During the present study, no complication like hematoma, laryngeal nerve palsy or perforation of trachea was noted. Evaluation of FNA smears was done according to the Bethesda system for reporting thyroid cytopathology. Out of 250 cases, histopathological correlation was done in 21 cases.

The number of males in present study were 22 (8.8%) and the females were 228 (91.2%) with M:F ratio 1:10.3 which was comparable with study of Gharia et al Mehrotra et al and Shankar et al and who showed M:F ratio of 1:7.7 1:9.3 and 1:8.3 respectively.[2,7,13] While in Sharma et al study M:F ratio was 1:5.2.[3]

In present study, maximum cases were of category II 219 (87.6%) cases which was comparable with studies conducted by Gharia et al, Shankar et al and Mehra et al. they showed 165 cases (82.5%), 328 cases (81.6%) and 180 cases (80 %) cases respectively in their study.[2,7,13]
Second highest cases were of category I, 13 cases (5.20%), which was correlated with studies conducted by Mehra et al and Shankar et al who reported 16 cases (7.2%) and 43 cases (10.7%) respectively.[7,13] Bukhari et al study have highest 13 cases (10.8%) of category I.[14] Several factors responsible for nondiagnostic FNAC results which including personal skill, the nature of the thyroid nodules, vascularity of thyroid lesion, criteria used to judge adequacy of the smears, and the cystic area of the nodule. [3] According to TBSRTC category III should not exceed more than 7%. In our study, there were 7(2.8%) cases of category III, which was within defined limit.

Histopathological correlation was possible in 21 cases. Out of this, one case of suspicious for medullary carcinoma, was operated in other hospital and histopathology report of which was traced and was correlated with cytopathology diagnosis. One case of cystic colloid goiter was diagnosed on histopathology as adenomatoid goiter with micropapillary carcinoma which was a false-negative result. This is due to very small size of malignant lesion which was not represented in aspirated material. This indicates limitation of FNAC in small sized lesion. False-negative cytopathological diagnosis is most common in cystic carcinomas, especially papillary carcinoma, where up to 60% of cases can be truly diagnosed on FNAC. Presence of cystic change in thyroid nodules is a common diagnostic pitfall in cytopathological diagnosis.[3]

In present study, one case of atypia of undetermined significance (TBSRTC category III) was diagnosed as adenomatoid goiter with degenerative changes on histopathology. This was due to degenerative changes in adenomatoid goiter with large nuclei having prominent nucleoli and degenerative changes in cytology smears. On histopathology it was correctly diagnosed as adenomatoid goiter with degenerative changes.

Cytological diagnosis was correlated with the histopathology and the efficacy of FNAC was estimated by using the methodology of Galen and Gambino by calculating various parameters.[6]

In present study, accuracy of thyroid FNAC was 95% which is comparable with studies conducted by Bagga et al and Haberal et al who showed accuracy of 96.2% and 91.9% respectively in their study.[12,15] Sensitivity of FNAC in our study was 85.7% similar results were obtained by Mehrrota et al, Haberal et al and Murati et al with sensitivity of 87.1%, 92.6% and 78.57% respectively.[6,15,16] Specificity in our study was 100% which is comparable with study conducted by Mehrrota et al and Bagga et al and Haberal et al who showed specificity of 100%, 91.6% and 90% respectively.[6,12,15]

**Conclusion**

Bethesda system for reporting of thyroid lesions is very helpful in categorizing thyroid lesions and avoiding confusion for clinicians as compared to previous diagnostic categories. TBSRTC monograph is briefly written in an easy-to-read format and has color photographs which help in cytological diagnosis. Standardized diagnostic systems for Thyroid FNAC reporting can make results easier to understand for clinicians and give clue for therapeutic action. However, The skill of person doing aspiration, location of target lesion, careful reporting FNAC is the key to true diagnosis and proper treatment in thyroid mass. In the modern era ancillary testing with Immunohistochemistry on the cell block preparation can also help cytologist to arrive correct cytological diagnosis.

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