Original Article

Appraisal of Cytohistomorphology of Papillary Carcinoma Thyroid and its Variants with Evaluation of Discrepant Cases

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Abstract

Background: Papillary carcinoma thyroid is the most commonly occurring thyroid neoplasm which can be diagnosed by its characteristic cytological features by fine-needle aspiration procedure. Due too few limitations in fine-needle aspiration cytology (FNAC) technique, there are false-positive and false-negative diagnoses in papillary carcinoma thyroid lesions. **Aim:** In our study, we would like to evaluate the accuracy of thyroid FNAC and to determine the reasons for cytopathological discrepancies. **Materials and Methods:** Two hundred and twenty-three cases were collected from archives of our Department of Pathology. Slides were retrieved for which cytohistopathology correlation differed and reviewed. Statistical analysis for False positive/ negative rates, positive predictive value, sensitivity and specificity were done. **Results:** For 170 cases, cytohistopathology correlation, 27 cases were discordant which accounted for 15.2% of false-negative rates. 87% sensitivity, 96.6% positive predictive value and 10.6% false positive were calculated. **Conclusion:** FNAC is a reliable screening procedure in spite of having few pitfalls. Awareness of these pitfalls, while reporting by cytopathologist can minimize false-positive and false-negative reporting on thyroid lesions.

Keywords: *Cytology, false-negative rate, false-positive rate, papillary thyroid carcinoma*

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Introduction

Thyroid cancer is the most common endocrine tumors in worldwide. Papillary thyroid carcinoma (PTC) is the most common histological type of malignant thyroid tumors. At presently, its incidence has being increasing, which is accounted for early detection by ultrasonography and fine-needle aspiration cytology (FNAC) technique.[1]

FNAC is the first line of diagnostic test for evaluating the all thyroid gland lesions. This technique is an efficient method of segregating patients who needs surgical intervention owing its simplicity, cost-effectiveness, and easily available with high sensitivity and specificity.[2]

There are well-established diagnostic criteria of PTC on FNAC and on histopathology. Despite of these advantages of FNAC and diagnostic criteria of PTC, FNAC can be limited by the quality of material. There are few worrisome possibilities of false-positive and false-negative results on cytology, which can have negative impact on patient care. The most common reasons for false positive results were because of the presence of similar features in various benign lesions of thyroid gland and the false-negative results were due to cases presenting with the absence of characteristic criteria of PTC or seen less frequently in cytology smears.[2,3]

Thus, in this study, we would like to evaluate the accuracy of thyroid FNAC and to determine the reasons for cytopathological discrepancies. We like to evaluate all the discordant cases and attempt will be made to minimize false-positive and false-negative diagnoses in PCT on FNAC.

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Materials and Methods

For our study, we collected samples from 2014 to 2019 from archives of Department of Pathology from our college. After obtaining Institutional Ethical Committee permission from our institution, the data were searched from cytology and histopathology records. All the cases reported as PTC either on cytology or histopathology was documented. The information about the age and sex of the patient, and cytology and histopathology diagnoses so as to study the age distribution of the tumor and correlation between the cytology and histopathology reports (HPR). Cases which did not correlate slides were retrieved and reviewed by two pathologists to look for cause of misdiagnosis.

Statistical analysis was done using SPSS software version 22 (IBM, Chicago, USA). Sensitivity, specificity, positive predictive value, false positive rate, and false negative rate were analyzed.

Results

In our study, there were 223 cases reported as PTC on cytology or histopathology. The cytological diagnosis of PTC was given in 194 cases, out of which proper diagnosis of PCT in 146 cases and suspicious of papillary carcinoma thyroid in 48 cases.

The histopathology diagnosis of PTC was given in 188 cases; cytohistopathological correlation was among 170 cases. In 27 cases, the cytology reports differed. This amounted to false-negative rate of 15.2%.

Cytohistopathological correlation [Table 1] was 80%. False–positive rate was 10.6% [Table 2] and false-negative rate was 15.2% [Table 3]. Sensitivity was 87% and positive predictive value was 96.6%. The peak age was 26–45 years and female (164 cases) to be predominant than male (59 cases).

Table 1: Cytohistopathological correlation

Histopathological diagnosis	Cytology diagnosis	Discordant cases
PCT - 173 cases	PCT - 120 cases (truepositive)	27 cases (false negative)
Nonpapillary ca (5 cases)	PCT - 5 cases	19 cases (false positive)

PCT: Papillary carcinoma thyroid

Table 2: Distribution of false positive cases on cytology

Number of cases (19 cases)	Cytological diagnosis	Histopathology diagnosis
4	Suspicious for PCT	HT
5	Suspicious for PCT	Nodular colloid goiter with micropapillary carcinoma
1	Suspicious for PCT	Nodular colloid goiter with secondary changes
8	Suspicious for PCT	Follicular adenoma
1	PTC	Mixed adenoma

PCT: Papillary carcinoma thyroid, HT: Hashimoto thyroiditis

Table 3: Distribution of false negative cases on cytology

Number of cases (27 cases)	Cytological diagnosis	Histopathology Diagnosis
2	HT	PCT
6	HT	Micropapillary Ca thyroid+HT
3	HT	PCT+HT
3	Cystic lesion	PCT
2	Nodular colloid goiter	PCT
5	Nodular colloid goiter	Micropapillary Ca thyroid+HT
6	Follicular lesions	Follicular variant of PCT

HT: Hashimoto thyroiditis, PCT: Papillary carcinoma thyroid

Discussion

Thyroid diseases are among the most common endocrine disorders worldwide. The National Cancer Registry Programme in India has reported thyroid as the most common site of cancer accounting for 1.5% of all cancers in men and 3.3% in women.[1]

Papillary carcinoma is the frequent type of all thyroid malignancy diagnosed usually at third to fifth decades of life. In our study, second to fourth decades range with female preponderance 73.5% commonly seen.[1]

Fine-needle aspiration of thyroid has gained popularity for initial diagnosis, since it is simple technique with reliable and time saving and cost effective. FNAC is regarded as Gold Standard since it is minimally invasive and can be done on outpatient basis. On cytology we can distinguish benign from neoplastic thyroid lesions, since FNAC has high diagnostic accuracy which has in turn reduced the incidence of surgical interventions.[2,3]

In spite of its advantageous properties, there exist certain limitations such as sample inadequacy, sampling techniques, worrisome histological alterations following fine-needle aspiration of the thyroid changes, false negative and false positive reports. Aware of these limitations will help the cytopathologist to reduce the errors while reporting.[3]

In the present study, cytohistopathological correlation was seen in 170 cases out of 225 cases. On cytology, "Suspicious for papillary carcinoma" diagnosis was made for 48 cases. Out of which, 26 cases confirmed as PTC on histopathology and 4 cases as well-differentiated carcinoma. The rest 19 cytology diagnosis did not correlate with HPR. On histopathology, four cases were Hashimoto's thyroiditis, five cases nodular colloid goiter

with micro papillary carcinoma, one case of nodular colloid goiter with secondary changes, eight cases of follicular adenoma, and one case of mixed adenoma. In this study, only PTC cases were selected; hence, there were no true negative cases and we could not calculate false positive rate, specificity, and negative predictive value. Thus, false-positive percentage of cytodiagnosis in our study was 10.6% as compared to other studies which ranged from 5.26% to 11.6%.[4-7]

This can be explained that pitfalls of FNACs in rendering confirmation of diagnosis in cases where there is a scarcity of characteristic features of PTC such as nuclear grooves, nuclear pseudoinclusions, and other features, which were less frequently seen in benign conditions of thyroid gland lesions such as Hashimoto's thyroiditis, adenomatous goiter, nodular colloid goiter, and follicular neoplasm. We observed same reasons of false-positive cases.[7-9] Many other studies have mentioned that these features in benign conditions are very less common to occur when compared to PTC.[7,9-12] Thus, the presence of characteristic features of PTC in these cases we reported them under "suspicious for papillary carcinoma." However, these 18 cases showed nuclear grooves in ten0 cases, eight cases showed intranuclear cytoplasmic inclusions in less number of cells, and these cases did not demonstrate psammoma bodies, metaplastic cytoplasm, or three dimensional fragments of PTC features. Awareness of cytopathologist about pitfalls of FNACs and strict adherence to adequacy criteria can reduce the false-positive rates.

Representative area sampling error or sample misinterpretation of cytology can lead to false-negative FNAC results. These reasons can account to miss a malignant lesion on cytology and are consider being gray zone of FNAC.[7,13,14]

In the present study, 27 cases with a diagnosis of PCT on HPE had been misinterpreted on cytology. False-negative rate in our study was 15.2% as compared to 4%–19% reported in other comparable research studies. False negative 9 cases of Hashimoto s thyroiditis on cytology found to be micropapillary carcinoma with Hashimoto's thyroiditis in six cases and PCT along with Hashimoto's thyroiditis in three cases. The word "micropapillary carcinoma" is an incidental findings, when tumor measuring <1 cm in diameter. Micropapillary carcinoma arising in Hashimoto's thyroiditis or PCT in Hashimoto's thyroiditis or in any other benign lesions has high chances of being missed on FNAC because FNAC is a blind technique, thus representative area sampling error can be frequently encountered.[15,16]

Diagnostically challenge in everyday practice to distinguish atypical nuclear changes that can be mistaken for foci of PTC for Hashimoto's thyroiditis diagnosis on cytology. Neoplasia incidence of diagnosis in setting of Hashimoto's thyroiditis by FNAC is 4%. The nuclei of thyroid follicular cells which are associated with lymphocytic infiltrates in Hashimoto's thyroiditis may show clearing of the nuclear chromatin and grooves which can be mistaken for PTC diagnosis.[14] Thus, sampling errors on cytology are mainly because of false-negative diagnosis of Hashimoto's thyroiditis.

In our study, six cases diagnosis as follicular neoplasia on cytology were confirmed on HPE as FVPTC. Characteristic nuclear features are very much necessary for the diagnosis of PTC which is infrequently seen on cytology smears for diagnosing FVPTC cases. It is difficult to diagnose on cytologically since nuclear features of PTC are seen in only few cells.[17] Other studies have reported that sensitivity of FNA in diagnosis of FVPTC is low and requires cytopathologist to consider infrequent nuclear features with follicular patter in cytology to consider the diagnosis of FVPTC, which is a major pitfall on cytology.[17-19]

False-negative FNAC diagnosis can also occur due to inadequate sampling or due to the cystic fluid aspiration of the thyroid gland with underlying malignancy, which can be seen in our three cases. PTC is known thyroid carcinoma to undergo remarkable degenerative changes. Sampling from these lesions will yield only sparse tumor cells which can result in false interpretation as benign cystic change. Hence, in such cases, surgical excision to rule out an underlying malignancy, advice by cytopathologist will led into timely surgery and halts the undue complications of PTC on patients.[20-22]

In our study, we found that, in spite of limitations on FNAC, it is a reliable technique of screening thyroid nodules for PTC with sensitivity as 87% and a positive predictive value of 96.6%. Our results are comparable with other studies where sensitivity ranged as low as 55.3% and false negative as low as 44.7%.

Conclusion

FNAC is a gold standard procedure and an indispensable tool for early diagnosis of all thyroid malignancies. Limitations of FNACs have led to false positive and false-negative diagnosis, especially in PTC thyroid. False-positive diagnosis can be reported due to the presence of characteristic features of PTC in benign conditions of thyroid gland. False-negative diagnosis has resulted due to inadequate sampling material like in cystic fluid or inadequate sampling area like in

micropapillary carcinoma of thyroid and in cases with coexisting with Hashimoto's thyroiditis cases and infrequent nuclear features of PTC, which can cause diagnostic dilemma such as in FVPTC.

Hence, awareness of various pitfalls of FNAC of thyroid lesions by cytopathologist can limit false-positive and false-negative diagnosis, which in turn would aid in choosing appropriate treatment modality and better patient care.

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Conflicts of interest

There are no conflicts of interest.

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