

Cytological Features in The Early Diagnosis Of Papillary Carcinoma Of Thyroid In Clinically Inapparent Cases

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ABSTRACT

Background: Papillary thyroid carcinoma (PTC) is the most common among the thyroid malignancies. Fine needle aspiration cytology (FNAC) is the first line investigation in the diagnosis of thyroid lesions. Here we review the significance of certain features conventionally considered to be diagnostic of papillary thyroid carcinoma on FNAC – including type of background, type of colloid, presence or absence of papillary clusters, intranuclear inclusions and nuclear grooves which were also considered for their importance in early diagnosis of PTC.

Methods: We reviewed all the thyroid FNACs performed over 18 months period and correlated them clinically and histopathologically, wherever available.

Results: Out of a total of 354 cases of thyroid FNACs, histopathological correlation was possible in 90 cases, with a concordant diagnosis in 82 cases. Analysis of the 8 discordant FNAC smears revealed papillary clusters along with nuclear features, especially nuclear grooves to be the most important finding in indicating a diagnosis of PTC.

Conclusion: Although the presence of papillary clusters along with characteristic nuclear features on FNAC is well known to indicate diagnosis of PTC, these findings can be easily missed on cytology smears, especially when the lesions are small (less than 1 cm) and diagnosis is clinically inapparent. Hence, we propose that the presence of papillary clusters in any case should alert the pathologist towards a diagnosis of PTC. A diligent search for nuclear features should follow. Thus a high index of suspicion while examining the FNAC smears in these patients will help in early detection of PTC.

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Introduction

Nodular tumors are the most common pathologies of the thyroid and they have been seen in up to 60 % of the population.^[1,2] As we know, papillary thyroid carcinoma (PTC) has been shown to be the most common malignant tumor of the thyroid.^[3] The pathological diagnosis and classification of PTC rests on the microscopic features of the specimens.

Fine needle aspiration (FNA) of the thyroid has now become a well-established method for initial evaluation of thyroid tumors, because of its high level of accuracy in predicting PTC (reaching up to 90%).^[4] However, the final diagnosis of benign or malignant nature of the tumor is based on the histopathological features of the tumor following resection.

Histological and cytological diagnosis of PTC has always been one of the most problematic dilemmas in surgical pathology. There are limited studies that specifically address details of cytologic features associated with cytohistologic discrepancy. Although cytomorphological features associated with PTC have been well defined by various authors (including papillary fronds, monolayered sheets, tissue fragments, intranuclear cytoplasmic inclusions, type of colloid, psammoma bodies, and multinucleated giant cells), none of the features alone is considered diagnostic for PTC. Various studies have shown that PTC is often underdiagnosed or overdiagnosed.^[5]

Materials and Methods

This was a retrospective study which included a total of 354 patients who underwent thyroid FNAC in the cytopathology laboratory of our institute over duration of 18 months. In each case, FNAC had been done with the help of a 23-gauge needle on a 10-ml syringe attached to a pistol-type handle. Smears had been prepared and immediately fixed in 90 % ethanol, and further stained with Papanicolaou and hematoxylin and eosin stains.

90 of the 354 cases had subsequently undergone surgery, and histological specimens were available in these cases. FNAC smears of all these patients were reviewed and correlated clinically and histopathologically, with special emphasis on cases showing histopathological diagnosis of PTC and discordant FNAC findings.

We aim to address the reliability and significance of certain cytological features in the diagnosis of PTC. These features are; Type of background, Type of colloid, Papillary fragments, Intranuclear inclusions, and Nuclear grooves.

We also suggest certain cytological features which would be helpful in the early diagnosis of PTC, i.e., diagnosing lesions that are less than 1 cm in size and not apparent clinically.

Result

Among 90 cases of thyroid cytology in which histopathological correlation was possible, eight had been diagnosed as PTC on histopathology, while they had been missed on cytology. We reviewed these eight cases in detail and found that most of them were females (7 of 8, 87.5%) younger than 35 years of age (6 of 8, 75%), and presented as a case of multinodular goiter (7 of 8, 87.5%). PTC was not suspected clinically in any of these cases.

Six cases were initially put in the category of non neoplastic thyroid lesions on cytology while two were labeled as unsatisfactory. On histopathological review, the diagnosis was changed to PTC in all eight cases with seven being the routine variant and one, the follicular variant of PTC. It is important to note here that most of these cases (6 of 8, 75%) were small lesions, with a maximum diameter of less than 1 cm.

The cytology slides of these eight cases were further studied in detail once more, especially noting five important features, i.e.: Background, Colloid, Papillary clusters, Nuclear grooves, and Intranuclear inclusion.

On studying the background, we noted that six of the cases (75%) had abundant normal epithelium in the background while two (25%) had scant cellularity in background (Fig.1). The colloid was scant in five of the eight cases (62.5%) while it was moderate in three cases (37.5%) (Fig.2). Papillary clusters proved to be an important criterion, noted in seven of the eight cases (87.5%) (Fig.3). Nuclear grooves were seen in five of the eight cases (62.5%) (Fig.4), while intranuclear inclusions were seen in only three cases (37.5 %) (Fig.5).

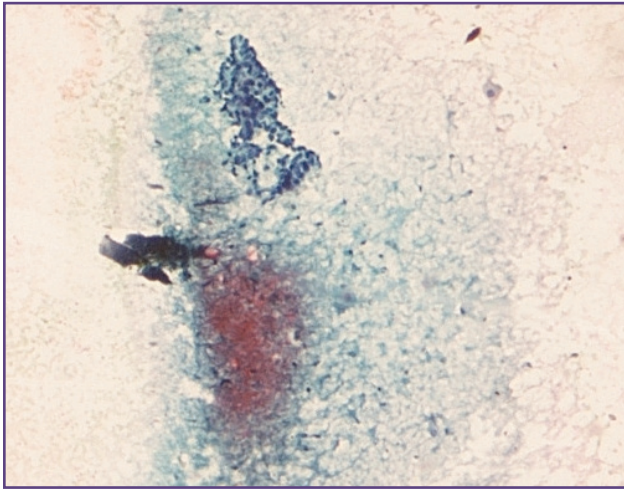


Fig. 1: Unsatisfactory smear with scant colloid and single cluster of cells with papillaroid arrangement (Pap, 4x)

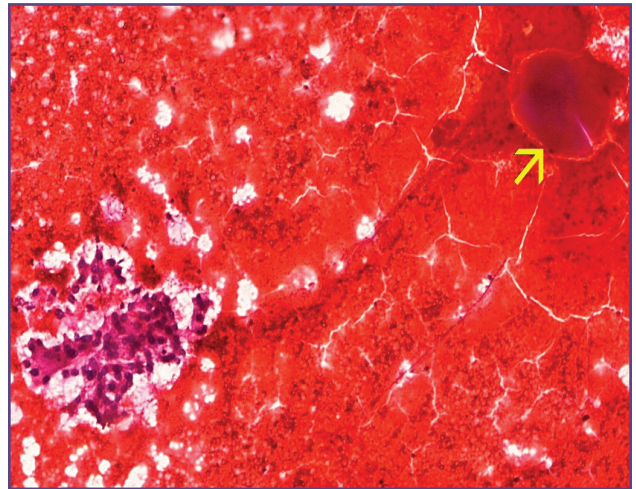


Fig. 2: Smear showing papillary fragment of follicular cells with thick colloid (arrow) (H&E, 10x)

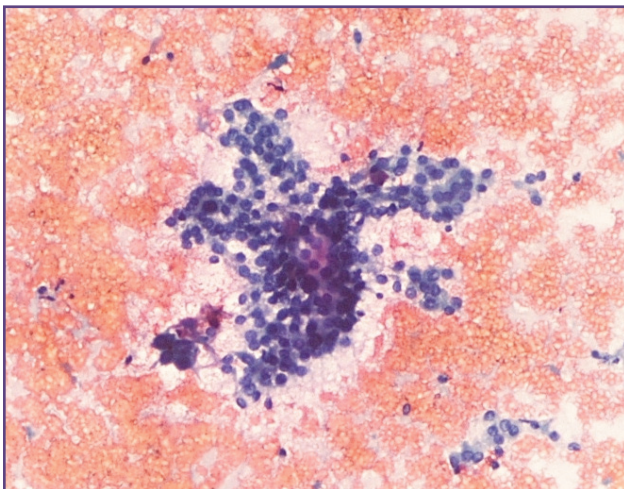


Fig. 3: Follicular cells arranged in papillary architecture (H&E, 10x)

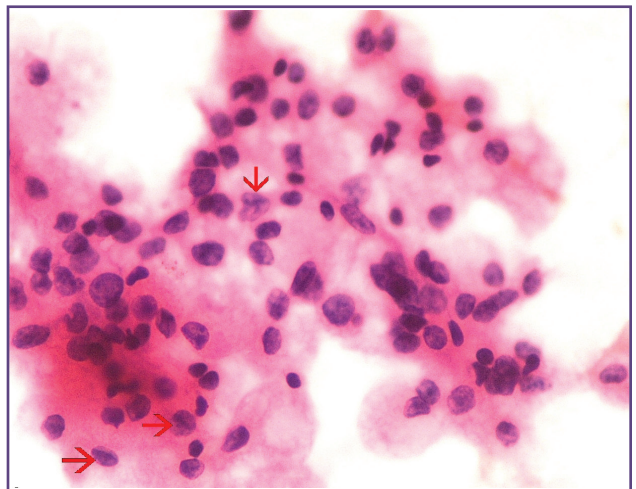


Fig. 4: Smear showing foamy cells in papillary carcinoma with nuclear grooves

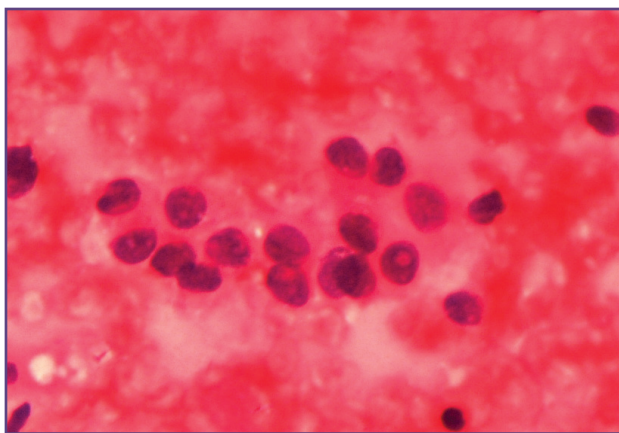


Fig. 5: Smear showing intranuclear inclusions (H&E, 40x)

Table 1 describes the initial FNAC diagnosis, histopathology findings and findings on review of cytology in the eight discordant cases.

Table 1: Initial FNAC diagnosis, histopathological findings and findings on review of FNAC smears in eight discordant cases

FINDINGS ON REVIEW OF FNAC SMEARS		
BACKGROUND	Scant	Abundant normal epithelium
No. of cases	2	6
COLLOID	Scant	Moderate, bubble gum type
No. of cases	5	3
PAPILLARY CLUSTERS	Present	Absent
No. of cases	7	1
NUCLEAR GROOVES	Present	Absent
No. of cases	5	3
INTRANUCLEAR INCLUSIONS	Present	Absent
No. of cases	3	5

Discussion

The management of thyroid nodules relies on the clinical presentation of the patient, tumor characteristics, and investigation findings, all of which must be considered when making a decision about the treatment approach. It is imperative to correlate the clinical context with radiology findings and, most importantly, findings on FNAB. While additional investigations such as immunostaining may be useful in the future; they do not play a major role in routine diagnostic process at present. The basic question the physician wants answered is whether the thyroid nodule is benign or malignant, to define the further management of the patient- active intervention or careful observation. Fine-needle aspiration biopsy is the most helpful diagnostic method and is now considered essential in the initial workup of any thyroid nodule. The cytological appearance of PTC has been well defined by different authors. Kini et al,^[6] described six parameters for PTC: Papillary tissue fragments, monolayer sheets of follicular cells, intranuclear cytoplasmic inclusions, nuclear grooves, tissue fragments with or without a follicular pattern, and large multinucleated foreign body-type of giant cells in the absence of degenerative changes.

According to Wu et al,^[7] the most frequent cytology findings in PTC were flat syncytial sheets, nuclear enlargement, fine chromatin, nuclear grooves, intranuclear cytoplasmic inclusions, and some amount of colloid. Castro-Gomez et al,^[8] described 15 features of PTC in FNA smears of thyroid: Tridimensional fragments, papillae, anisonucleosis, nuclear bars (grooves), intranuclear cytoplasmic inclusions, powdery chromatin, vacuolated cytoplasm, metaplastic cytoplasm, psammoma bodies, autolysis, multinucleated giant cells, spindle cells, colloid, monolayer lamina, and macrophages. Kumar et al,^[9] suggested cellular swirls in cytology smears are highly specific for PTC. Despite these well-defined cytology features, diagnosis of PTC on cytology is often difficult and currently, no international standard exists for the cytological diagnosis of PTC.

Recently, extensive studies have been done on these cytological criteria of PTC and their usefulness has been significantly debated. Christine R. Fraser et al described 3 cases with hypercellularity and papillary fragments on FNAB, suggesting a diagnosis of PTC but which were later found to be benign on histology.^[10] In our study, we found that 87.5% of the cases of PTC showed papillary clusters.

Gould et al. found in their study that 100% of the papillary carcinomas contained nuclear grooves while only 70% contained inclusions. Grooves, however, could be seen in 70% of nonpapillary neoplasms and in 56% of nonneoplastic conditions of the thyroid also. Inclusions were present in 13% of nonpapillary neoplasms and were absent in nonneoplastic conditions.^[11] In comparison, we found nuclear grooves and intranuclear inclusions in 62.5% and 37.5% of the cases of PTC respectively.

Psammoma bodies can also be a confusing feature as it can be found in PTC as well as many benign conditions like multinodular goiter. Erin Ellison et al found in their study that psammoma bodies were as predictive of multinodular goiter as PTC.^[12]

Keeping in mind the previous published reports on this topic combined with our own findings in this study, we have found papillary clusters along with nuclear features especially nuclear grooves, to be the most important finding in indicating a diagnosis of

PTC. These features should alert the pathologist to the possibility of a diagnosis of papillary carcinoma of the thyroid, even in cases which are not primarily suspected to have PTC clinically. However, none of these features are diagnostic on their own and a thorough study of all the cytological features and their correlation is necessary in each case.

Conclusion

The presence of papillary clusters along with characteristic nuclear features on FNAC is well known to indicate a diagnosis of PTC. However, we noted in our study that these findings can be easily missed on cytology smears, especially when the lesions are small (less than 1 cm), and the diagnosis is not apparent clinically. We conclude that presence of papillary clusters on FNAC in a young female patient should alert the pathologist to a possibility of PTC, and trigger a diligent search for nuclear features. Such a practice will help in early detection of PTC even before they become clinically apparent, thus leading to adequate management of the patients and improved prognosis.

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Competing Interests

none declared

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