 DOI: 10.18231/2394-6792.2017.0004

To evaluate the role of cellular swirls in fine needle aspiration cytology diagnosis of papillary carcinoma thyroid

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Abstract

Objective: To enhance the diagnostic accuracy of papillary carcinoma thyroid by evaluating nuclear and architectural features on cytology with address about the details of cytologic pitfalls.

Study Design: 14 cases of papillary carcinoma thyroid diagnosed on FNA cytology, which were confirmed on histology, during last five years, were reviewed, retrospectively, using Papanicolaou stained and May Grunwald Geimsa stained slides for following parameters-

Architecture: Papillary pattern, swirling pattern, follicular pattern, sheets. Nuclear features: nuclear inclusion, nuclear grooving, and powdery chromatin. Others: metaplastic cells, chewing gum colloid, cystic macrophage, multinucleated giant cells.

Result: Out of the various features evaluated the most consistent findings were papillary and swirling pattern; nuclear inclusion and nuclear grooving and metaplastic cells.In our study, on an average intranuclear grooves were present in 30-40% of the follicular epithelial cells except in one case where it was 80-90%. The average of intranuclear pseudoinclusions was 3-5% in all cases except one where it was 32%. Other findings were multinucleated giant cells, cystic macrophages, chewing gum colloid.

Conclusion: Diagnosis of papillary carcinoma thyroid can be made accurately if architectural features (papillary or swirling pattern, nuclear features (nuclear inclusions and grooves) and metaplastic cells are present together in a thyroid aspirate. Among architectural features swirling pattern is consistent finding in our study which could be included among diagnostic criteria.

Keywords: FNAC Thyroid; Papillary Carcinoma; Swirling Pattern.

Introduction

In recent years, FNA has proven to be a rapid cost effective and well tolerated tool in the selection of thyroid nodule patients requiring surgical intervention, halving the number of patients undergoing thyroid surgery and doubling the incidence of malignancy in the resected specimens. Although the cytological features of papillary carcinoma of thyroid are well defined on FNA but none of the single cytological feature is pathognomic for the diagnosis, constellation of cytological features are required. In addition to multiple cytological features,[1-5] swirling architectural pattern[6] can be an important morphological predictor of papillary carcinoma on FNAC.

We reviewed 14 histologically proven cases of papillary carcinoma thyroid retrospectively on cytology and specifically addressed about the details of cytologic pitfalls.

Materials and Methods

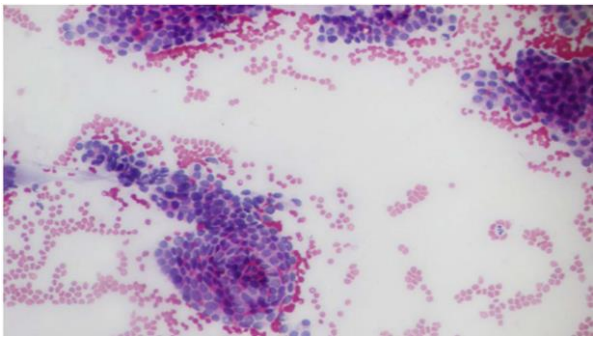
14 already proven cases of papillary carcinoma thyroid on histology were reviewed retrospectively on cytology and were evaluated on papanicolaou stained and May Grunwald Geimsa stained slides using following parameters and criteria for them

Architecture: papillary pattern, swirling pattern, follicular pattern, sheets.

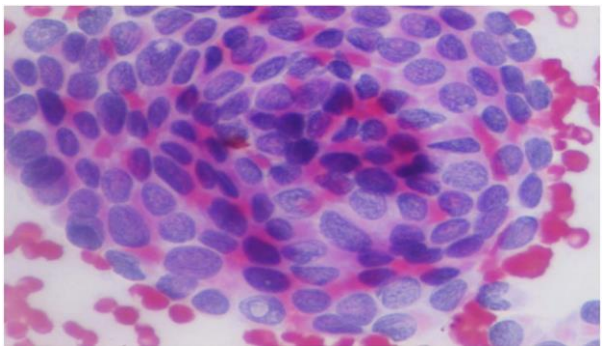
Nuclear features: nuclear inclusion, nuclear grooving, powdery chromatin.

Others: metaplastic cells, chewing gum colloid, cystic macrophages, multi-nucleated giant cells.

Swirling pattern: These structures are relatively flat rather than ball-like and did not contain any colloid. Cellular swirls consisted of concentrically organized aggregates of about 50–200 tumor cells, in which most of the peripherally situated cells have ovoid rather than round nuclei, the long axes of which were oriented perpendicular to the radius of the swirl (Fig. 1a, b).



a



b

Fig. 1a, b: Papillary carcinoma, swirls concentrically arranged tumor cells forming swirls with peripherally located cells appearing perpendicular to radius of the swirls (Pap a- 100X;b- 400 X)

Papillae: Varying in shapes, sizes but show a smooth surface contour, peripheral palisading of the surface cells. The core which is less visualized and made up of small amount of fibrous tissue containing small blood vessels (Fig. 2). *Microfollicular pattern*: Cells arranged peripherally in tubular fashion with central small lumen containing colloid (Fig. 3).

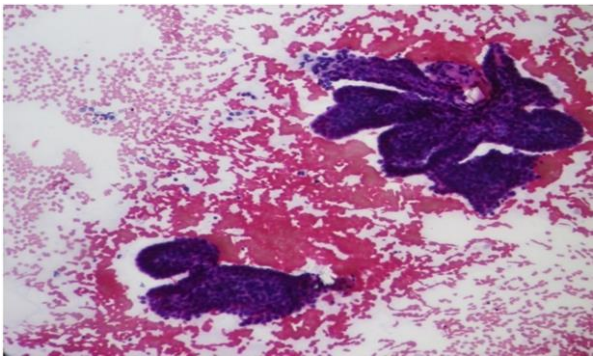


Fig. 2: Papillary carcinoma papillary fragments, finger- like papillae with anatomical edges (Pap- 100 X)

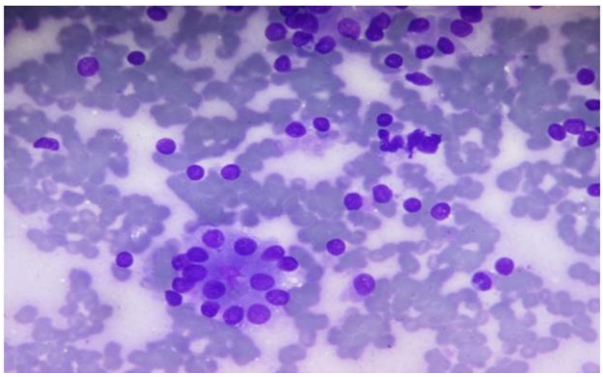


Fig. 3: Cells arranged peripherally in tubular fashion with central small lumen containing colloid- Microfollicular pattern (MGG- 400 X)

Sheets: *Monolayered sheet*: Many cells arranged side by side cohesively containing moderate amount of eosinophillic cytoplasm displaying well defined cytoplasmic borders and evenly distributed nuclei with minimal overlapping- *honeycomb* sheet(Fig. 4). And s*yncytial- type sheet*- In this cytoplasmic border of Cells in sheet not well defined and the nuclei show crowding/ overlapping/ molding.

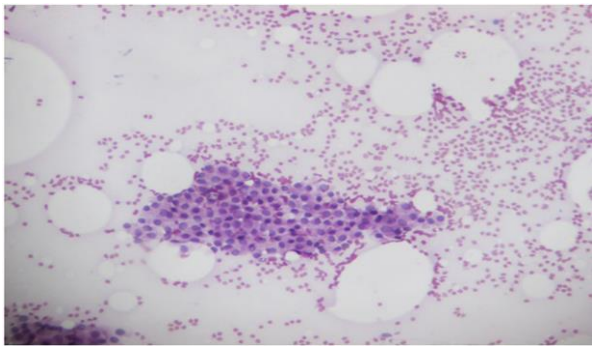


Fig. 4: Monolayered honeycomb sheet: Many cells arranged side by side cohesively displaying minimal overlapping containing moderate amount of eosinophillic cytoplasm (Pap-100 X)

Intranuclear pseudoinclusion also called "nuclear cytoplasmic Inclusion" (INCI): Well-defined empty looking round or oval regular areas of pallor in the follicular epithelial cell nuclei. They usually occupy at least one –third of the nuclear area and contain material apparently similar to cytoplasm of cells (Fig. 5). The INCI appears as a grayish/light- greenish hue with touch of hyaline or ground glass appearance in Papanicolaou stained smears and pink/magenta staining in May Grunwald- Giemsa stained smears. And the intensity of staining varies depending on the thickness of the nuclear envelope over the inclusion.

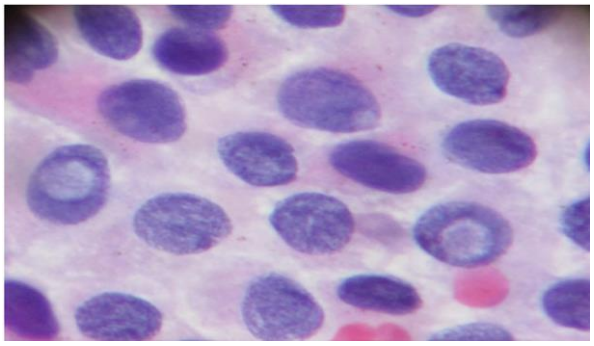


Fig. 5: Nuclear pseudoinclusion: Well defined empty looking round or oval regular central pallor in the follicular epithelial cell nuclei occupying at least one third of the nuclear area and contain material apparently similar to cytoplasm of cells (H & E- 400 X)

Nuclear grooving (NG): Nuclear membrane invagination traversing the entire longitudinal axis of the nucleus (Fig. 6). *Powdery chromatin*: Fine granular chromatin (Fig. 7).

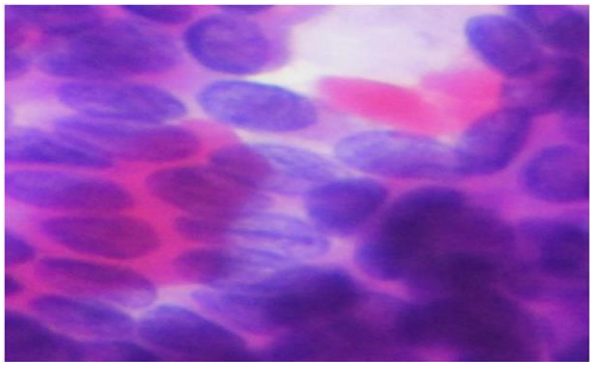


Fig. 6: Papillary carcinoma: Sheets of cells with crowded nuclei, powdery chromatin and longitudinal grooves (Pap- 400 X)

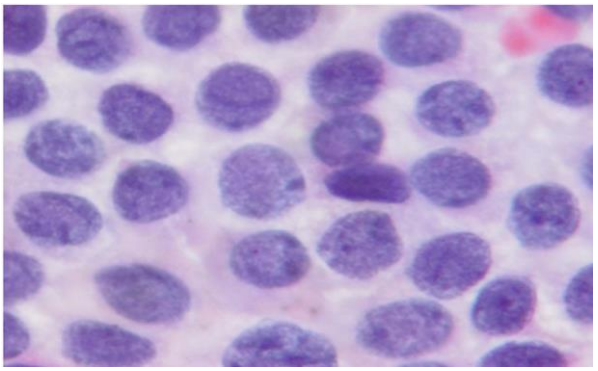


Fig. 7: Powdery chromatin: fine granular chromatin (Pap- 400 X)

Chewing gum colloid: Scant, viscous colloid and appears as irregular thickness or dense blobs (Fig. 8).

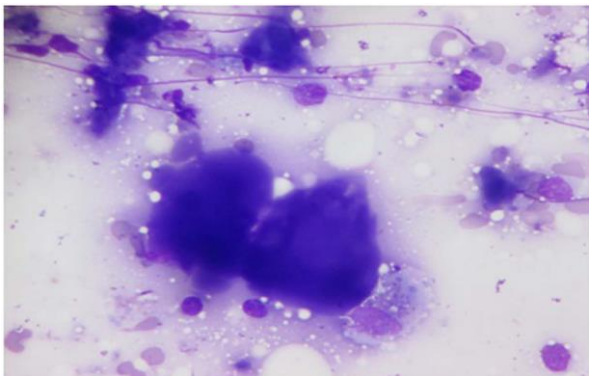


Fig. 8: Chewing gum colloid: Scant, viscous colloid and appears as irregular thickness or dense blobs (H&E-400 X)

Metaplastic cell: Cells with well-defined borders having moderate amount of dense cytoplasm displaying round to oval bland nuclei (Fig. 9).

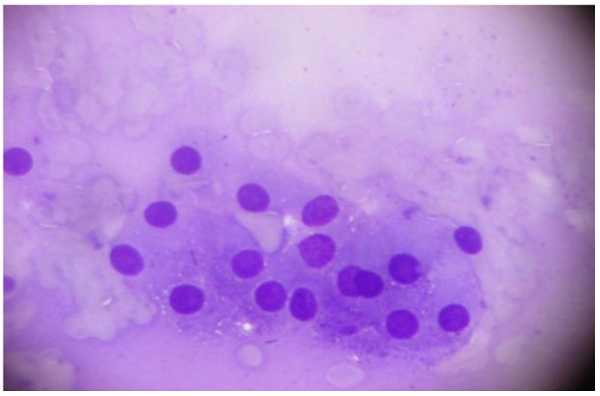


Fig. 9: Metaplastic cells: Cells with well defined borders having moderate amount of dense cytoplasm displaying round to oval bland nuclei (MGG- 400 X)

Giant cells: Most common foreign body type are adjacent to papillary or monolayer fragments of tumor cells (Fig. 10).

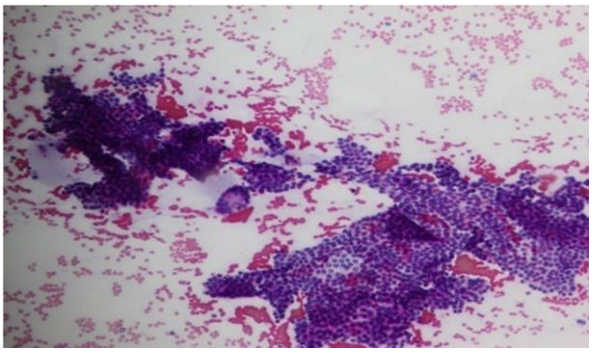


Fig. 10: Giant cells: Most common foreign body type lying adjacent to papillary or monolayer fragments of tumor cell (Pap a-100 X; b- 400 X)

Histiocytoid cells/ Histiocytes: Elongated oval nuclei with vacuolated cytoplasm (Fig. 11).

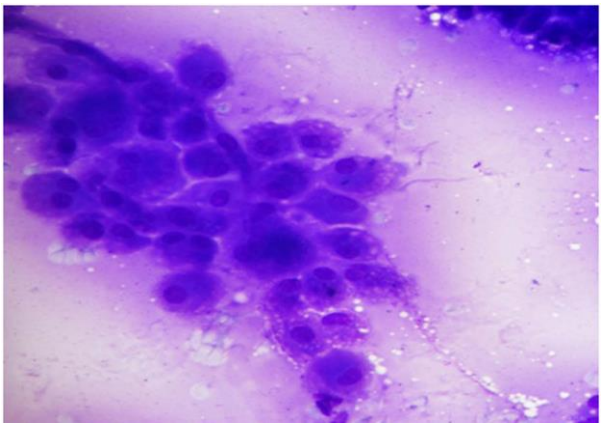


Fig. 11: Histiocytes: Elongated oval nuclei with vacuolated cytoplasm (MGG- 400 X)

Result

Out of the various features evaluated the most frequent/ predominant pattern was papillary fragments (9/ 14 cases), syncytial sheet (4/14) and least predominant pattern was swirling pattern which was consistently present in all the cases. In one case microfollicular pattern was predominant pattern- diagnosed as microfollicular variant of PTC on histology (Table 1). Nuclear inclusion and nuclear grooving and powdery chromatin were present in all cases. Nuclear grooving is more abundant than nuclear inclusion (Table 2, 3). In our study, on an average nuclear groove was present in 30-40% of the follicular epithelial cells except in one case where it was 80-90%. The average of nuclear inclusions was 3-5% in all cases except one where it was 32%. Other common findings were multinucleated giant cells (11/14), cystic macrophages/ histiocytes (10/14) and metaplastic cells (11/14) (Table 3).

Table 1: +4 Most Predominant; +3 Second Most Predominant; +2THIRD MOST Predominant;+1 Least

Architecture	4	3	2	1	Present in total no of cases
Swirling			1	13	14
Papillae	9	2	2	1	14
Sheets	4	7	3		14
Microfollicular	1	7	5		13

Table 2

Nuclear Feature	+3	+2	+1	Total
*Nuclear Grooving	2	9	3	14
*Nuclear Pseudoinclusion	----	1	13	14

*NG +1 -0%-30%/10hpf; +2- 31%-60%/10hpf; +3- >60%/10 hpf

Table 3

Feature	No. of Cases Present	No. of Cases Absent
Powdery Chromatin	14	--
Giant Cells	11	3
Hitiocytes	10	4
Metaplastic Cells	11	3

Discussion

The cytological features of papillary carcinoma thyroid (PTC) on FNA material is well described but there exists a group of cases in which other thyroid lesions can mimic nuclear-cytological features or architectural pattern posing diagnostic problem. Papillary structures can be found in other lesions also like Grave's disease, hyperplastic nodules and adenomas but lack nuclear features of PTC.[7] Jing X and Michael C W pointed out that papillary- like fragments in benign thyroid lesions reveal honeycomb pattern with well- defined cytoplasmic borders (easily made out on mid-high power microscopy) and evenly distributed nuclei whereas papillary fragments of PTC exhibit syncytial arrangement with unevenly distributed nuclei, nuclear crowding, and/or nuclear overlapping.[8] WHO has described a distinctive set of nuclear characteristics for the diagnosis of papillary carcinoma.[9] Intranuclear grooves within follicular epithelial cells are of diagnostic help but not specific for papillary carcinoma of thyroid as it is seen in other thyroid lesions also such as lymphocytic thyroiditis, follicular adenoma, follicular carcinoma, nodular goitre, hashimoto's disease and medullary carcinoma.[10-11] Thick/ longitudinal intranuclear grooves accompanied by other cytological features- architectural/ nuclear atypia is important criteria for true PTC whereas it is thin and/ or incomplete in benign entities.[8] Further pitfalls due to orientation of nucleus: such as to view the groove on edge can cause confusion and the invagination is appreciated as a notch. According to quantification studies –papillary carcinoma tends to have higher number of cells possessing intranuclear grooves than other thyroid lesions[12] and its presence in a widespread pattern can be considered a reliable criteria.[8] Alkumari E et al suggested that presence of >20% of cells, as counted in selected fields where grooves are frequent, which is highly predictive of papillary carcinoma of thyroid.[13] Intranuclear pseudoinclusions (INCIs) are due to cytoplasmic invagination and are hallmark for papillary carcinoma, although not in all cases, as it can be seen in other lesions including multinodular goiter, hyalinizing trabecular adenoma, Hashimoto's thyroiditis, insular carcinoma and medullary carcinoma.[10-12] Different stages of transition from membrane indentation, simple groove to complex pockets may be seen. And beside usual round or oval shape of INCI, other shape like: drop/flask- shaped, planoconvex/semicircular, and rectangular forms are less commonly seen.[14] And there are also some pitfalls: 1. Artifacts- intranuclear pseudoinclusion tend to be small, 2. Nuclei with clear holes not containing cytoplasm- like material, usually contains biotin and the outer boundary of the hole is not sharp, 3. Orientation of the cells to the observer: off angle inclusion may not show sharply defined edge due to nucleoplasm between observer and the inclusion.[7] According to Yang GC et al in 1997 suggested that if more than three (>3) INCIs are seen in enlarged nuclei on a single aspirate of a thyroid nodule, the finding is almost pathognomic for a papillary carcinoma.[15] Further INCIs are more frequent in tall cell/ columnar variant of PTC but in follicular variant of papillary CA INCIs are fewer in number and not well developed. So specific number of INCI is not a prerequisite for the diagnosis of PTC but the absence of INCI increases potential for misdiagnosis.[7] According to Kini 2008 "The minimal criteria for the diagnosis of papillary carcinoma"- includes: syncytial type tissue fragment of

follicular epithelium that, regardless of the architectural pattern, shows a typical nuclear morphology, that is, pale appearing enlarged nuclei with fine, dusty, powdery chromatin; a chromatin bar or ridge; single or multiple micro- and/ or macronucleoli; and INCIs.[16] Das D K et al, in 2009 found that the presence of ≥ 3 of the following features-papillae, psamomma bodies, nuclear groove, inclusions and granular chromatin has been reported to facilitate cytological diagnosis of papillary carcinoma of thyroid with frequent grooves and inclusions being the most dependable.[17] Miller T R et al –logistic regression analysis of various criteria suggested that a combination of intranuclear cytoplasmic pseudo inclusion, papillary structure without adherent blood vessels and dense metaplastic cytoplasm were the most important variables. A combination of any of these two gave 100% predictive value.[18] Kumar S *et al*, in 2010 found cellular swirls as novel findings and when present in cytological smears, are highly specific for PTC.[19] Swirling pattern was described first by Szoporn 2006 and suggested that it can be included as one of the diagnostic criteria for better diagnosis and reproducibility of papillary carcinoma thyroid on cytology.[6] Yashawani R et al 2015 have done retrospective Cyto-histological correlation of 30 cases of PTC and concluded that cellular swirls are novel findings and when present in cytology smears, are highly specific for PTC and it is a useful additional cytological finding in PTC.[20] In our study all PTC cases showed cellular swirls (Table 1). Nuclear grooves and inclusions were present in all cases (Table 2). 10 out of 14 cases show presence of histiocytes. Psamomma bodies were seen in none of the cases (Table 3).

Conclusion

Diagnosis of papillary carcinoma thyroid can be made accurately if combination of architectural features (papillary or swirling pattern), nuclear features (nuclear inclusions and groove) are present together in a thyroid aspirate. And the swirling pattern can be included as one of the diagnostic criteria for enhancing diagnosis of papillary carcinoma on fine needle cytological aspirates.

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