Study of various nuclear features of papillary thyroid carcinoma in other thyroid lesions

Manjula K[1,*], CSBR Prasad[2], Harendra Kumar ML[3]

[1]Associate Professor, [2]Professor and HOD, [3]Principal, Dept. of Pathology, Sri Devaraj URS Medical College, Kolar, Karnataka, India

***Corresponding Author:**
Email: gkpmanju966@rediffmail.com

Abstract

Introduction: Papillary thyroid carcinoma is the only thyroid malignancy that is diagnosed on the basis of its nuclear characteristics, regardless of cytoplasmic features, growth patterns or immunohistochemistry.

Although nuclear features have become hallmark for the diagnosis, they are neither constant nor specific. They can be seen in other tumours and non-tumours condition of thyroid. With the aim to know the frequency of various nuclear features of papillary thyroid carcinoma in other thyroid lesions and also to find out which of the various nuclear features are most diagnostic of papillary thyroid carcinoma, this study was done.

Materials and Methods: The present study was conducted on Fine needle aspiration cytology of thyroid lesions where corresponding histopathological diagnosis was available, from 2010 to 2016. All cytology smears of were reviewed by two investigators who were blinded with respect to the final histopathological diagnosis.

Results: 155 cases were included in the study; category 2 was the most common constituting 76%, followed by category 6 which was 35%. Frequency of various nuclear features of papillary carcinoma in other thyroid categories varied from 10% to 33%.

Conclusion: Frequency of various nuclear features of papillary carcinoma in other thyroid categories varied from 10% to 33% and Intranuclear cytoplasmic inclusions are the most diagnostic nuclear features of papillary carcinoma.

Keywords: Papillary thyroid carcinoma, Nuclear inclusions, Nuclear grooves, Fine granular chromatin.

Introduction

Papillary thyroid carcinoma is the only thyroid malignancy that is diagnosed on the basis of its nuclear characteristics, regardless of cytoplasmic features, growth patterns or immunohistochemistry.[1] The diagnosis of Papillary Thyroid Carcinoma (PTC) depends on presence of major diagnostic nuclear features. These are enlarged crowded nuclei, fine powdery chromatin, Intranuclear cytoplasmic inclusions (INCI), nuclear grooves, micro or macronucleoli.[1-3]

Although nuclear features have become hallmark for the diagnosis, they are neither constant nor specific. They can be seen in many other conditions like hashimotos thyrioditis, nodular goiter, in other primary thyroid tumors (medullary carcinoma hurthle cell neoplasms) and also in secondary tumors (malignant melanoma, bronchioalveolar carcinoma, and ovarian tumors).[4,5]

This study was carried out to know the frequency of various nuclear features of papillary thyroid carcinoma in other thyroid lesions and to find out which of the various nuclear features are most diagnostic of papillary thyroid carcinoma

Materials and Methods

The present study was conducted on 155 cases of Fine needle aspiration cytology of thyroid lesions where corresponding histopathological diagnosis was available, from 2010 to 2016 in the department of pathology attached to SDUAHER. All cytology smears of were reviewed by two investigators who were blinded with respect to the final histopathological diagnosis. All smears were reexamined under low power field for the degree of cellularity, cell arrangement and amount of colloid. Each papanicolaou stained smear was carefully examined semi quantitatively under high power field (HPF) for the presence of various nuclear features. Minimum 20 cellular HPF were examined for the presence of nuclear crowding, enlarged irregular nuclei, fine granular chromatin, nuclear grooves, INCI. A score of 1 + was given if any nuclear feature was present, 2+ when nuclear feature were more than 5HPF, 3+ when nuclear feature were more than 10 HPF. All cases were reviewed based on Bethesda system for reporting thyroid cytopathology. The microscopic findings studied were entered in Microsoft office excel sheet, descriptive statistical analysis was done.

Results

The study was conducted on 155cases of fine needle aspirations of thyroid. Category 2-76 cases, category 3-14 cases, category 4-18 cases, category 5-12 cases, category 6-35 cases. Age range was from 24-61 years. Male to female ratio was 1:5. Category 1 was excluded from the study.

Frequency of various nuclear features in all categories is shown in Table 1 and 2. Enlarged crowded nuclei were seen in 100% of PTC, where score+1, +2 were 57.14, and +3 42.85. In other thyroid categories category 3- 16.6%, category 4- 25.0% and enlarged crowded nuclei were not seen in category 1 and 2.

Fine granular (powdery) chromatin was present in all PTC. Score+ 1 and +2 were seen in 80% and +3 in 20%. In other thyroid categories, category 2 had 15.7% (score+1), category 3- 21.4% (score +1), category 4- 27.7%, (score+1) category 5- 33% (Score+1). INCI were seen in 100% of PTC. INCI+1, +2 were seen in 82.3% and +3- 5.7%. INCI were not found in other thyroid categories

Nuclear grooves in papillary thyroid score +1, +2 were seen in 85.71% and +3- 14.28%. Category 5 had 20%, not seen other categories.

85% (+1) of PTC showed micronuleoli, in other categories category 2 – 10%, category 3 -21.4%, category 4- 16.6%, category 5 -33%.

Table 1: Various nuclear features in category 2, 3, 4 and 5

Cytological features	Cat -2 n=76	Percentage	Cat 3 n=14	%	Cat -4 n=18	%	Cat -5 n=12	%	Chi-Squar	p-value
Crowded enlarged nucleus+1	0		0		3	16.66	0			
Fine granular chromatin+1	12	15.78	3	21.4	5	27.77	4	33.0	42.04	0.001
Nuclear grooves+1	0		0		0		3	25	39.01	0.001
INCI	0		0		0		0			
Micronuclei+1	8	10	3	21.4	3	16.6	4	33.0	36.67	0.0001

Table 2: **Various nuclear features of papillary carcinoma in category 6**

Cytomorphological features	Cat -6 n=35	Percentage	Chi Squar	p-value
Enlarged crowded nucleus+1and +2	20	57.14		
Enlarged crowded nucleus+3	15	42.85		
Fine granular chromatin+1 and+2	28	80.0		
Fine granular chromatin +3	7	20.0		
Nuclear grooves+1and +2	30	85.71	127.01	0.0001
Nuclear grooves+3	5	14.28		
INCI+1and +2	28	80.0	125.01	0.0001
INCI +3	4	11.42		
Micro nucleoli+1	30	85	130.03	0.0001

Discussion

Papillary thyroid carcinoma is the most common thyroid malignancy accounting to 80% of all thyroid carcinomas; they are more common in female. Most commonly seen below 40 years of age, it is the most common pediatric thyroid tumor[1,4,6]

The diagnosis of papillary carcinoma on Fine needle cytology depends on presence of well recognized nuclear features irrespective of architectural pattern. They should be presenting widespread throughout the follicular cell population. Papillary carcinoma is the only tumor that is diagnosed based of nuclear features.[7]

The most common nuclear features are enlarged crowded nuclei, fine powdery chromatin, INCI, nuclear grooves and micro or macronucleoli. However these nuclear features lack specificity, they can be seen in many benign and malignant conditions of thyroid and also in others secondary tumors.[1,4,5,8] Present study aimed to know the frequency of various nuclear features of papillary thyroid carcinoma in other thyroid lesions and to find out which of the various nuclear features are most diagnostic of papillary thyroid carcinoma. Table 3 compares various nuclear features of papillary carcinoma with other studies.

Table 3: Comparison of present study category 6 with other studies

Nuclear features	Mallik MK et al n=61	Politi HD et al n=37	Mittendorf EA et al n=45	Bhat A et al n=21	Rani D et al n=32	Present study n=35
crowded enlarged nucleus	97%		77	100	97	100
Fine granular chromatin	95%	95%		100	100	100
Nuclear grooves	55%	92%	94.4	100	46	100
INCI	93%	92%	94.4	23	93	91.42
Micronucleoli					53	85

In the present study, all the aspirates of papillary carcinoma showed enlarged crowded nuclei (Fig 1). 57.14% of papillary carcinoma showed score+1 and +2, and score 3+ was 42.85%. Similar to our study, enlarged crowded nuclei were significant findings in a study done by Bhat A et al,[9] Rani et al,[10] and Kunjumon

and Upadhyaya,[11] where they reported that enlarged crowded nuclei were seen in 100% of papillary carcinoma cases.

Fine granular (powdery) chromatin (Fig. 2) was present in all the papillary thyroid carcinoma. + 1 and +2 were seen in 80% and +3 in 20%. Similar finding were noted by Bhat A et al[9] and Rani et al[10] where they have reported 100% of PTC had fine granular chromatin. This chromatin change can be seen in aspirates containing large amount of peripheral blood, which hinders proper fixation of smears, can be avoided by using thinner gauge needle and limiting number of passes.[12]

Intranuclear cytoplasmic inclusions are the most valuable diagnostic nuclear Feature of papillary carcinoma (Fig. 3). It was first reported by Soderstrom and Biorkland in 1973.[13] These are crisp, clear, can vary in number; margins are usually sharp and distinct. Density and texture is similar to the cytoplasm, better seen in Papanicolaou stains.[1,4,14,] Presence of more than three intranuclear inclusions seen in enlarged nuclei on a single thyroid aspirate is diagnostic of papillary thyroid carcinoma.[15] These should not be confused for clear areas in the nucleus which are usually artifacts.[1, 13,15,16] In the present study INCI+1, +2 were seen in82.3% and 5.7% (+3) and not found in other thyroid categories. P valve was 0.0001, highly significant. Rani et al[10] in her study reported in 93.8% cases of papillary thyroid carcinoma. Kini et al[17] in 83% of histologically proven papillary thyroid cancer, and while Sharma et al[18] in 86.5% of cases. Studies have shown that they can be seen in benign non papillary thyroid lesions.[19,20] In a study done by Pandey et al,[21] where they have studied 447 thyroid aspirates, the reason behind wrong diagnosis of some cases was due to too much emphasis on intranuclear inclusions and they have told that although typical nuclear alterations help in the diagnosis of PTC, none of them are diagnostic in isolation or low frequency. They are diagnostic when they are widespread and in combination.

Nuclear grooves (Fig. 2 and 4) which are nothing but invagination of the nuclear membrane that will traverse the entire longitudinal axis of the nucleus are another important nuclear feature of papillary carcinoma.[1,4,5 22] In the present study, in papillary carcinoma nuclear grooves +1, +2 was seen in 87.71% and +3 14.28% (+3). P valve was 0.0001 highly significant. Bhat et al[10] in her study had similar results, in other studies frequency varies from 46% to 94%. Nuclear grooves in other thyroid categories were shown in table 1. In a study done by Mallik et al,[8] nuclear grooves were not seen in category 2 and 4, while category 5 had -20% and they have said that grooves can be regarded as useful cytomorphological feature in the diagnosis of papillary thyroid carcinoma. Sharma et al[18] observed in 78% of papillary thyroid carcinoma. In a study done by Politi HD[22] nuclear grooves were seen in 92% of papillary carcinoma thyroid, only two of 50 caese of follicular neoplasms, they were present in small number and the authors believed that nuclear grooves were a very useful criterion in the diagnosis of PTC by fine needle aspiration biopsy. In a study done by Scopa CD et al,[23] they have said that nuclear groves are not restricted to papillary carcinoma, they can present in various thyroid lesions.

Nucleolus may be small and large, Can be single or multiple. In the present study 85% (+1) of papillary carcinoma showed micronuleoli (Fig. 4). In other studies, Bhat A et al[9] had 100%, Rani et al[10] 53.1%.

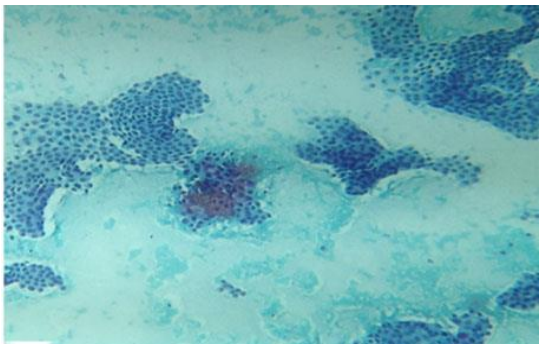

Fig. 1: Fine needle aspiration cytology smear showing follicular cells with enlarged crowded nuclei in a papillary fragment. (Papanicolaou stain, x200)

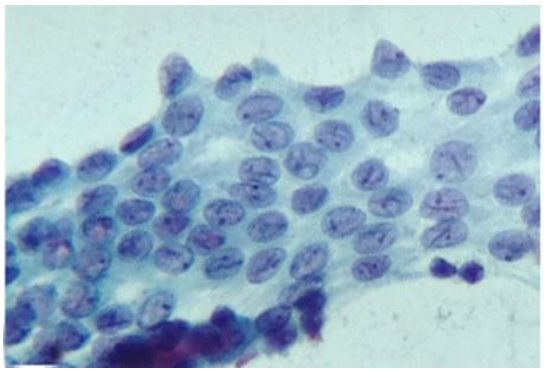

Fig. 2: Smear showing follicular cells with fine powdery granular chromatin and nuclear grooves. (Papanicolaou stain, x400)

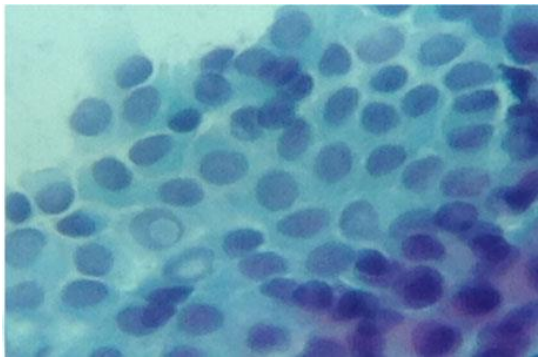

Fig. 3: Smear showing follicular cells with INCI. (Papanicolaou stain, x400)

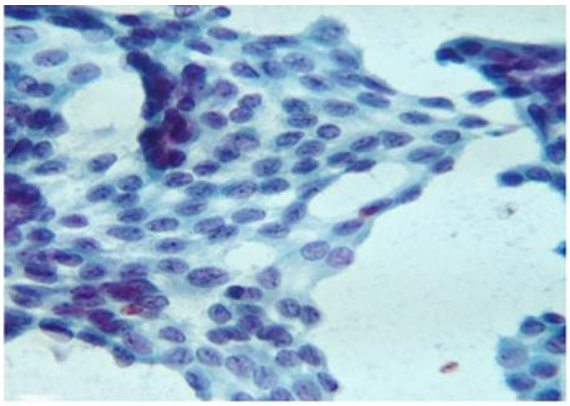

Fig. 4: Papillary fragment showing follicular cells with nuclear groove and micronuclei. (Papanicolaou stain, x400)

Conclusion

Various nuclear features of papillary carcinoma can be seen in other lesions of thyroid, but the percentage is really less. When strict morphological feature of each nuclear feature is kept in mind and seen the smears, they help in categorization and diagnosis of papillary carcinoma. The diagnosis of PTC should be based on all nuclear features rather than single feature. From the present study, we conclude that frequency of various nuclear features of papillary carcinoma in other thyroid categories varied from 10% to 33% and intranuclear cytoplasmic inclusions are the most diagnostic nuclear features of papillary carcinoma.

Conflicts of Interest: Nil

References

1. Baloch ZW et al. Diagnostic terminology and morphologic criteria for cytologic diagnosis of thyroid lesions: A synopsis of the national cancer institute thyroid fine needle aspiration state of the science conference. *Diag Cytopathol.* 2008;36(6):425-437.
2. Yang GC, Liebeskind D, Messina AV. Diagnostic accuracy of follicular variant of papillary thyroid carcinoma in fine needle aspirates processed by ultrafast papanicolaou stain: histopathologic followup of 125 cases. *Cancer*. 2006;108(3):174-179.
3. Das DK et all. Papillary thyroid carcinoma and its variants in fine needle aspiration aspiration smears. A cytomorphological study with special reference to tall cell variant. *Act Cytol.* 2004;48(3):325-336.
4. Miguel A, Sanchez, Stahl RE: The thyroid, Parathyroid, and Neckmasses other than lymph nodes. Koss diagnostic cytology and its histopathologic bases, Lippincott Williams and Wilkins 2006. 1162-1167
5. Davidson HG, Campora RG: Thyroid. Comprehensive cytopathology, Saunders, 2008. 650-654.
6. Oertel YC. Fine needle aspiration in the evaluation of thyroid neoplasms. *Endocr Pathol.*1997;8;215-224.
7. Cibas ES. Thyroid. Cytology diagnostic principles and clinical correlates, Elsevier saunders. 2014.282-286
8. Mallik MK et al. Dark and pale cerebriform nuclei in FNA smears of usual papillary thyroid carcinoma and its variants. *Diagn Cytopathol*. 2004;30(3):187-192.
9. Bhat A, Varma L, Fernands H, Jayaprakash CS. Papillary carcinoma thyroid –A cytomorphological study. *Journal of Pathology of Nepal.* 2016; 6(12):1005-1007
10. Rani D, Gupta a, Agarwal S, Bharati R. Cytomorphological study of papillary thyroid carcinoma; Acase study. *J Biol Sci Med.* 2016;2:1-9.
11. Kunjumon DT, Upadhyaya K. Histopathological feratures of papillary thyroid carcinoma with special emphasis on the significance of nuclear features in their diagnosis. *Archives of medicine and health sciences*. 2014;2(1):16-22.
12. Baloch ZW, LiVolsi VA. Cytologic and architectural mimics of papillary thyroid carcinoma. Diagnostic challenges on fine needle aspiration and surgical specimens. *Am J Clin Pathol.* 2006;125(suppl)S135-144.
13. Soderstrom N, Biorklund A. Intranuclear cytoplasmic inclusions in some type of thyroid cancer. *Acta Cytol.* 1973;17(3):191-197.
14. Kini SR. Guides to clinical aspiration biopsy thyroid. New York, Igaku Shoin, 1996.
15. Yang GC, Greenebaum E. clear nuclei of papillary thyroid carcinoma are conspicuous in fine needle aspiration and intraoperative smears processed by ultrafast Papanicolaou stain. *Mod Pathol.* 1997;10(6):552-555.
16. Gupta PK, Baloch ZW. Intraoperative and on site cytopathology consultation: utilization, limitations and value. *Semin Diagn Pathol*. 2002;19(4):227-236.
17. Kini SR, Miller JM, Hamburger JI et al. cytopathology of papillary thyroid carcinoma by fine needle aspiration. *Acta Cytol.* 1980;24(6):511-521.
18. Sharma B et al. Cytogiagnosis of papillary thyroid carcinoma study of 37 cases at RIMS hospital. *Indian J Pathol Microbiol.* 2007;50(2):408-410.
19. Glant MD, Berger EK, Davey DD. Intranuclear cytoplasmic inclusions in aspirates of follicular neoplasms of the thyrod. A report of two cases. *Acta Cytol.* 1984;28(5):576-580.
20. Lew W, Orell S, Henderson DW. Intranuclear vacuoles in nonpapillary carcinoma of the thyroid. A report of three cases. *Acta Cytol*. 1984; 28(5):581-586.
21. Pandey P, Dixit A, Mahajan NC. Fine needle aspiration of the thyroid: A cytohistologic correlation with critical evaluation of discordant cases. *Thyroid Research and Practice.* 2012;9(2):34-38.
22. Politi HD. Nuclear crease as a cytodiagnostic feature of papillary thyroid carcinoma in fine needle aspiration biopsies. *Diag Cytopathol*. 1987;3(4):307-310.
23. Scope CD, Melachrinou M, Saradopoulou C, Merino MJ. The significance of the grooved nucleus in thyroid lesions. *Mod Pathol*. 1993;6(6):691-694.

How to cite this article: Manjula K, Prasad CSBR, Kumar HML. Study of various nuclear features of papillary thyroid carcinoma in other thyroid lesions. J Diagn Pathol Oncol. 2018;4(3):141-144.