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Original Article

The diagnostic role of CK19 and CD73 immunohistochemistry in the diagnosis of papillary thyroid carcinoma

Pathology

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ABSTRACT:

Background: The presence of diagnostic doubt in specific thyroid lesions has been extensively recorded, even among pathologists with significant expertise. This is particularly true in cases of papillary thyroid cancer (PTC), where the nuclear characteristics may be unclear. Recently, numerous molecular variations in thyroid cancer have been employed to differentiate between malignant and benign thyroid tumors. Cytokeratin 19 (CK19) and cluster differentiation 73 (CD73) biomarkers have been successfully implemented in clinical practice, leading to a substantial enhancement in the preoperative diagnosis of thyroid cancer.

Objective: To assess the role of CK19 and CD73 in the diagnosis of PTC.

Methodology: This hospital-based cross-sectional study took place at, New Damietta and Al-Zahraa University Hospitals. The study included 60 cases of papillary thyroid carcinoma and twelve non-neoplastic cases. The presence of immunoreactivity in each marker was evaluated and scored as negative if there was no staining or weak staining in less than 10% of the cells. Any other immunoreactivity was recorded as positive.

Results: CK 19 had higher sensitivity but lowest specificity than CD73. While combination had lower specificity than CK19 alone and a sensitivity of 100%.

Conclusion: Ck19 or the combination of both markers could provide the best sensitivity, while CD73 provides the best specificity at 41%.

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Keywords: Papillary thyroid carcinoma; CK19; CD73; immunohistochemistry; PTC.

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INTRODUCTION

The microscopic differentiation between malignant and benign thyroid nodules with traditional histology is unpredictable. Papillary thyroid carcinoma represent more than 80% of palpable malignant thyroid nodules [1]. The presence of diagnostic doubt in specific thyroid lesions has been extensively recorded, even among pathologists with significant expertise. This is particularly true in cases with papillary thyroid cancer, where the nuclear characteristics can be unclear or open to interpretation [2]. The identification of low-grade malignancies, specifically papillary microcarcinoma, has significantly increased. This poses a genuine risk of overdiagnosis and overtreatment of these types of tumors [3].

Recently, numerous molecular variations in thyroid cancer have been employed to differentiate between malignant and benign thyroid tumors. Biomarkers, such as Cytokeratin 19 (CK19) and Cluster differentiation 73 (CD73), have been applied in clinical practice to greatly enhance the preoperative diagnosis of thyroid cancer [4]. Cytokeratin 19 is expressed in several cancers, such as liver, pancreatic, and gastric carcinoma [5]. The CD73/adenosine pathway is also active within the tumor microenvironment. The presence of CD73 on both tumor cells and stromal cells inhibits the immune system's ability to mount an effective antitumor response, hence facilitating tumor growth and the advancement of cancer [6]. The study aims to assess the diagnostic role of

Immunohistochemical expression of CK19 and CD73 in the diagnosis of Papillary Thyroid Carcinoma.

SUBJECTS AND METHOD

Study Design

Hospital based cross-sectional study conducted at Al-Azhar University Hospital, New Damietta, and Al-Zahraa University Hospital

Specimens selection

In the present study, we enrolled 72 thyroid specimens referred to our pathology department after total thyroidectomy. They were selected, based on the histopathological diagnosis. Clinical and demographic data were gathered from hospital records. The samples consisted of 60 cases of papillary thyroid cancer and twelve instances of non-neoplastic patients. The non-neoplastic suspicious group was of (Hashimoto thyroiditis and hyperplastic lesions), which was chosen because they exhibited certain shared characteristics with papillary thyroid cancer, such as papillary architecture or nuclear features.

Sample size calculation

Based on papillary thyroid carcinoma prevalence of (6%) among the Egyptian population from previous studies [7], the sample size required for the study was estimated with Open Epi 7, to be 60 patients at least, considering a confidence level of 90% and a power of 80% with α error 10%.

Methods

Each specimen included in the study was subjected to the following:

- **Histopathological reviewing**

The resected samples were preserved in a solution of 10% neutral buffered formalin with a pH of 7.4. They were then embedded in paraffin, sliced into sections that were 5 micrometers thick, and stained using the hematoxylin and eosin (HandE) method. Classification of thyroid tumors according to WHO classification 4th edition [8]. The staging of thyroid carcinoma is determined according to the AJCC 8th edition cancer staging criteria [9].

- **Evaluation of selected specimen sample**

- Personal and clinical data were collected from the patient's medical records including (Age, sex, Operational type, tumor size, and Histologic variants).
- Histopathologic examination of Hematoxylin and eosin stain (H and E) stained slides.

- **Immunohistochemical markers**

I. **CK19** (mouse monoclonal antihuman antibody (sc-53258; 1:50; Santa Cruz biotechnology, CA, USA))
II. **CD73** (mouse monoclonal antibody (1:100, ab71322 Abcam).

- **Immunohistochemical assessment**

The cells were considered positive for these markers when clear immunoreactivity was found in their cell membrane and/or cytoplasm. The immunoreactivity of each marker was assessed and scored as negative if there was no staining or weak staining in less than 10% of the cells. Any other immunoreactivity was rated as positive [10].

- **Scoring system for immunomarkers**

CK19: A semi-quantitative assessment of immunohistochemical scoring was performed. Immunoreactivity was deemed positive for all antibodies when more than 10% of follicular epithelial cells exhibited membranous and/or cytoplasmic staining. The immunoreactivity was evaluated and categorized as negative, focally positive (+: less than 25% of cells showing reactivity), positive (++: 25–50% of cells showing reactivity), or diffusely positive (+++: more than 50% of cells showing reactivity), based on the overall amount of the reaction [11].

CD73: The evaluation was assessed based on the degree of staining intensity and the proportion of cells that were stained either membranous and/or cytoplasmic. The scoring estimations were divided into four categories as follows: +++, which represents 20-49% of cells that are moderate to intensely stained or ≥50% of cells that are positively stained; ++, which represents 10-19% of cells that are intensively stained or 20-49% of cells that are weakly stained; +, which represents 10-19% of cells that are weakly to moderately stained; ±, which represents less than 10% of cells that are positively stained; and -, which represents 0% of cells that are positively stained. Positive values were recorded as + and above, while negative values were scored as -.

CD73 intensity: The staining intensity is classified as mild with a value of 1 or 1.5, moderate with a value of 2, and high with a value of 2.5 or 3 [12].

Statistical analysis

The data were gathered, organized, and subjected to statistical analysis using "Statistical Package for the Social Sciences (SPSS) version 27" software. We used 5% as cutoff for statistical test significant. For testing significant difference between categorical data, we used chi square test, while for continuous normally distributed data we compare mean with independent t-test.

RESULTS

In the present study, we summarize sample characteristics in table (1). Table (2) illustrates that seven cases of suspicious groups (58.3 %) showed membranous and/or cytoplasmic positive CD73 expression, while 57 (95. %) cases of PTC were positive with significant differences. In the PTC group, 30 (50%) cases showed moderate Scores while in the suspicious group, 6 (50%) have mild intensity with a significant difference higher score in the PTC

group**.** Eight cases (66.7 %)of the suspicious group showed membranous and/or cytoplasmic positive CK 19 expressions while 60 (100%) cases of PTC were positive with significant differences in positive frequency in the PTC group**.** In the PTC group, 53 (88.3%) cases showed a score of 3 while in the suspicious group, 7 (58.3%) have a score of one with a significant difference higher score in the PTC group as shown in table (2).

As shown in table (3) CK 19 had higher sensitivity but the lowest specificity than CD73. While combination had lower specificity than CK19 alone and a sensitivity of 100%. In table (4) we demonstrate that there were significant associations between CD73 Intensity and the studied clinicopathological parameters. There were no significant associations between CK19 Score and the studied clinicopathological parameters, except the histology type was significant.

Table (1): Demographic properties of the studied sample

Items		Total n = 72	Suspicious n = 12	PTC n = 60	P-value
Age (yrs.) [Mean ± SD] #		45.8± 12.7	36.3± 11.1	47.7 ± 12.2	0.04*
Sex [no. (%)]^	**Female**	54 (75%)	10 (83.3%)	44 (73.3%)	0.5
	Male	18 (25%)	2 (16.7%)	16 (26.7%)	
Operation^	**To talk**	47 (65.3%)	7 (58.3%)	40 (66.7%)	0.6
	Hemi	25 (34.7%)	5 (41.7%)	20 (33.3%)	

PTC: Papillary thyroid carcinoma, SD: Standard deviation, #: Student- t-test, ^: Chi square test, *: Significant p-value (0<.05)

Table (2): Immunohistochemistry expression in PTC and suspicious groups

		Suspicious n = 12 no. (%)	PTC n = 60 no. (%)	P-Value
CD73				
Status	**Negative**	**5 (41.7%)**	**3 (5%)**	0.001*
	Positive	**7 (58.3%)**	**57 (95%)**	
Score	**Mild**	6 (50%)	18 (30%)	0.001*
	Moderate	1 (8.3%)	30 (50%)	
	Strong	0 (0%)	9 (15%)	
CK 19				
Status	**Negative**	4 (33.3%)	0 (0%)	0.001*
	Positive	8 (66.7%)	60 (100%)	
Score	**Mild**	7 (58.3%)	0 (0%)	0.001*
	Moderate	1 (8.3%)	7 (11.1%)	
	Strong	0 (0%)	53 (88.3%)	

PTC: Papillary thyroid carcinoma, N: Number, CK: cytokeratin, CD: Custer differentiation, *: Significant p-value (0<.05), regarding score, we calculate the % in each group from the total number of cases in each group

Table (3): The diagnostic accuracy of CD73 and CK19 expression in diagnosing PTC

	Sensitivity	Specificity	PPV	NPV	Accuracy
CD73	95%	41.7%	89.1%	62.5%	86.1%
CK19	100%	33.3%	88.2%	100%	88.9%
CD73+CK19	100%	16.7%	85.7%	100%	86.1%

PPV: Positive predictive value, NPV: Negative predictive value, CK: Cytokeratin, CD: Cluster differentiation, *: Significant p-value (0<.05)

Table (4): The correlation between CD73, CK19 Intensity and the studied clinicopathological parameters among papillary thyroid cancer group

CD73 Intensity		Mild n= 18 no. (%)	Moderate n= 30 no. (%)	Strong n= 9 no. (%)	p- value
Histology type	Classic	18 (100%)	27 (90%)	4 (44.4%)	0.03*
	Follicular	0 (0%)	2 (6.7%)	3 (33.3%)	
	Warthin	0 (0%)	1 (3.3%)	1 (11.1%)	
	Oncocytic	0 (0%)	0 (0%)	1 (11.1%)	
Necrosis	Absent	18 (100%)	30 (100%)	4 (44.4%)	0.01*
	Present	0 (0%)	0 (0%)	5 (55.6%)	
Size	>2 cm	2 (11.1%)	22 (73.3%)	8 (88.9%)	0.01*
	<2 cm	16 (88.9%)	8 (26.7%)	1 (11.1%)	
LN status	Yes	0 (0%)	16 (53.3%)	6 (66.7%)	0.01*
	No	18 (100%)	14 (46. %)	3 (33.3%)	
CK19 score			**Moderate (n= 7) no. (%)**	**Strong (n= 53) no. (%)**	**p-value**
Histology type	Classic		2 (28.6%)	50 (94.3)	0.01*
	Follicular		2 (28.6%)	3(5.7)	
	Warthin		2 (28.6%)	0 (0%)	
	Oncocytic		1 (14.3%)	0 (0%)	
Necrosis	Absent		7 (100%)	48 (90.6%)	0.39
	Present		0 (0%)	5 (9.4%)	
Size	>2 cm		4 (57.1%)	28 (52.8%)	0.83
	<2 cm		3 (42.9%)	25 (47.2%)	
LN status	Yes		2 (28.6%)	20 (37.7%)	0.63
	No		5 (71.4%)	33 (62.3%)	

LN: Lymph node, CK: Cytokeratin, CD: Cluster differentiation, *: Significant p-value (0<.05)

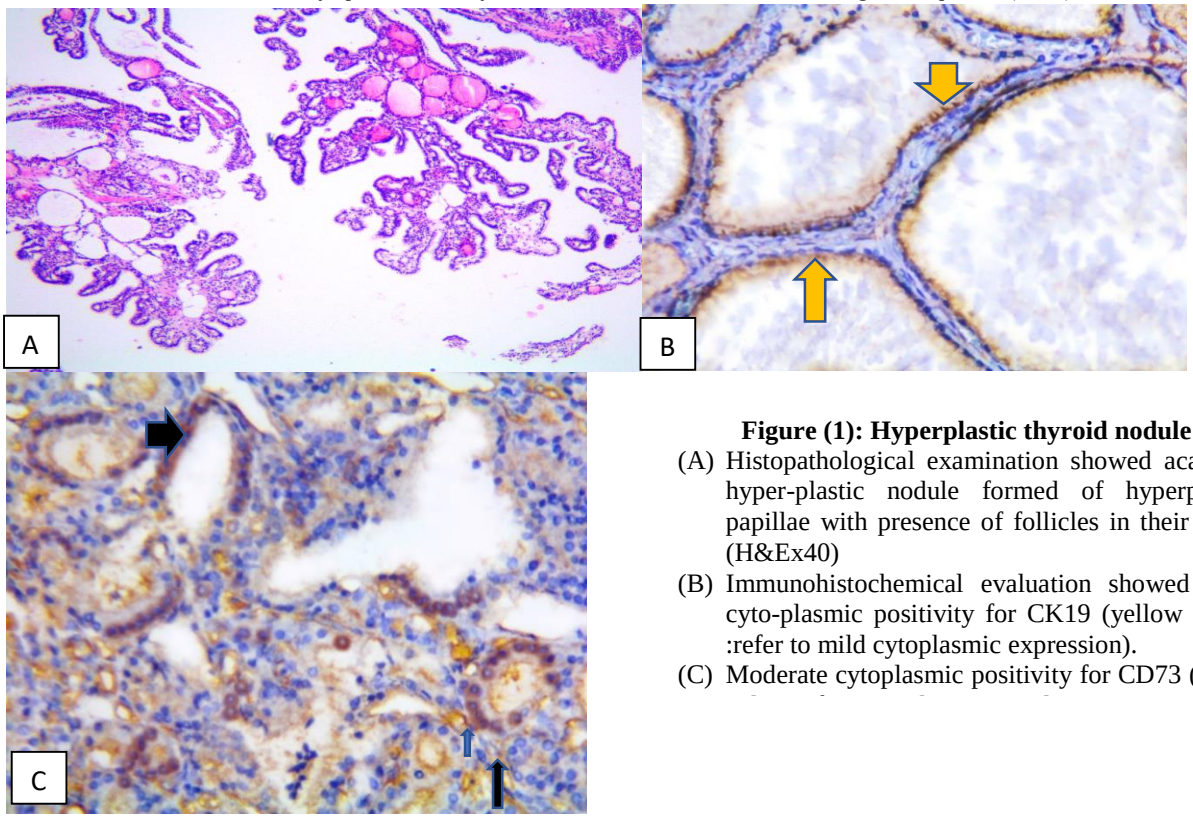


Figure (1): Hyperplastic thyroid nodule

(A) Histopathological examination showed acase of hyper-plastic nodule formed of hyperplastic papillae with presence of follicles in their cores (H&Ex40)

(B) Immunohistochemical evaluation showed mild cyto-plasmic positivity for CK19 (yellow arrow :refer to mild cytoplasmic expression).

(C) Moderate cytoplasmic positivity for CD73 (black

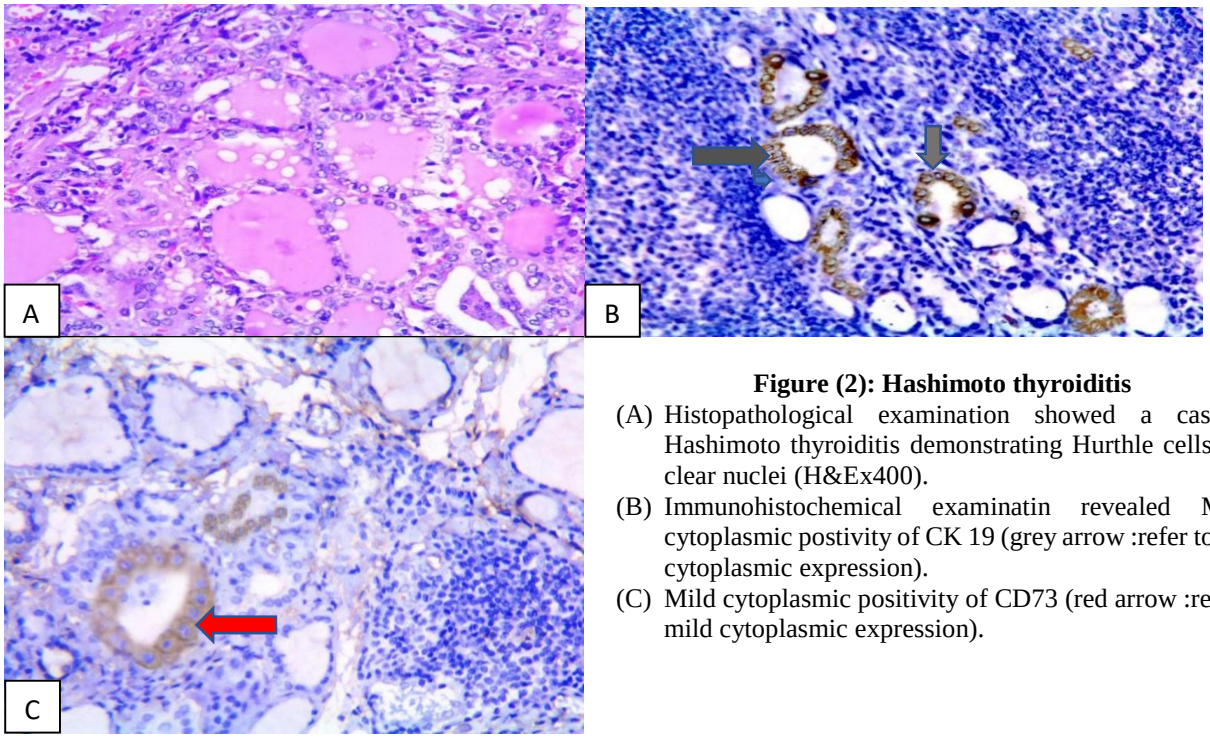


Figure (2): Hashimoto thyroiditis

(A) Histopathological examination showed a case of Hashimoto thyroiditis demonstrating Hurthle cells with clear nuclei (H&Ex400).
(B) Immunohistochemical examinatin revealed MILD cytoplasmic postivity of CK 19 (grey arrow :refer to mild cytoplasmic expression).
(C) Mild cytoplasmic positivity of CD73 (red arrow :refer to mild cytoplasmic expression).

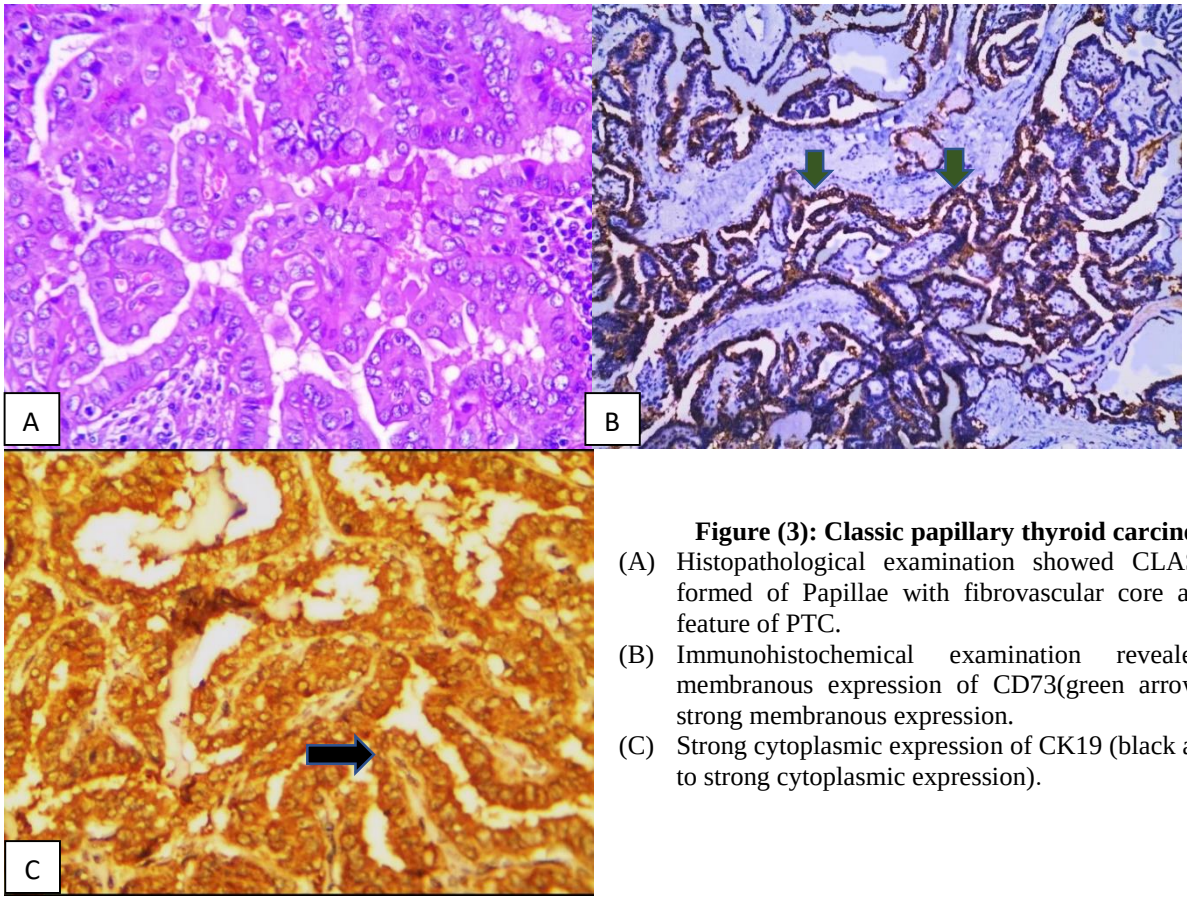
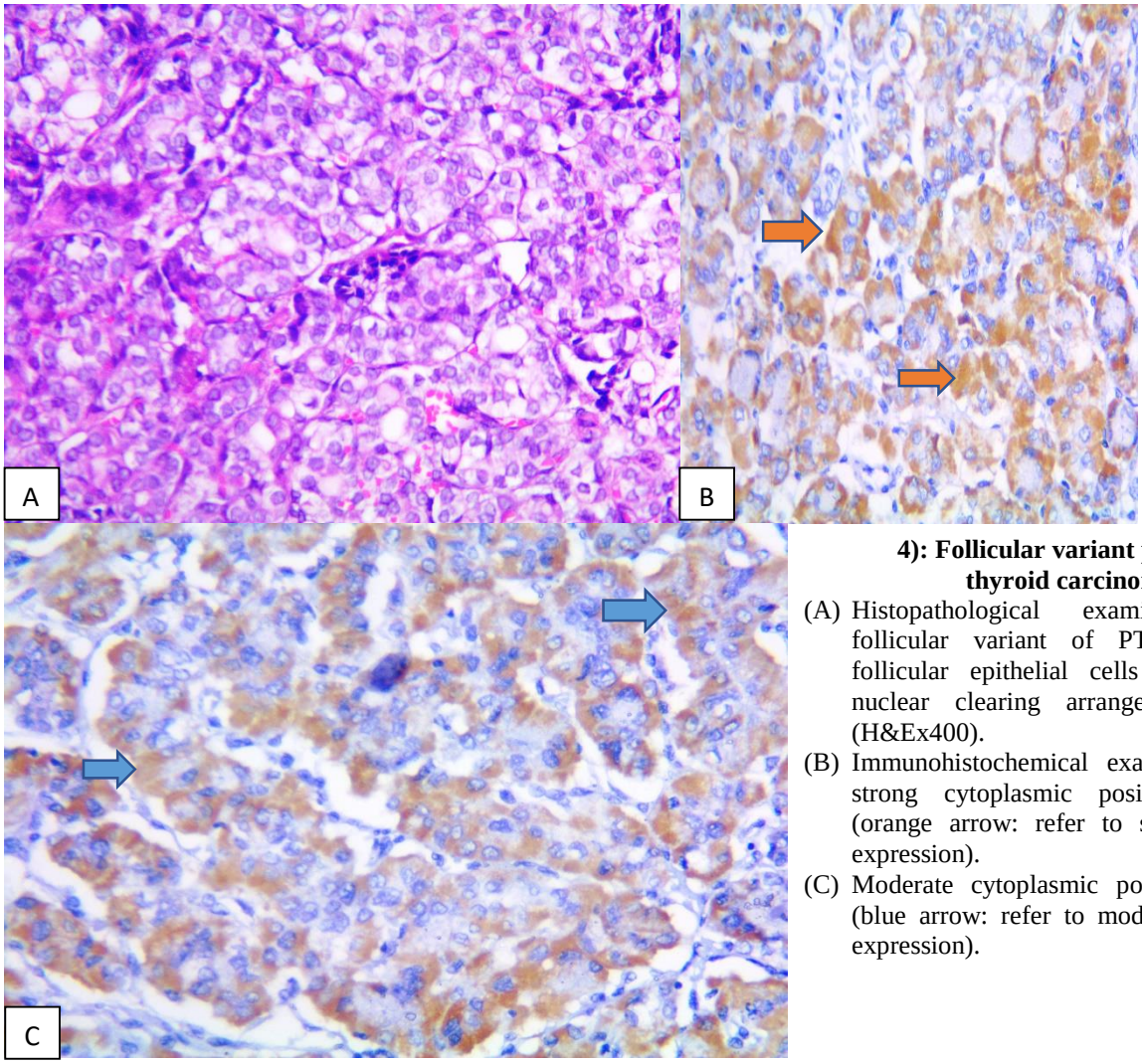


Figure (3): Classic papillary thyroid carcinoma

(A) Histopathological examination showed CLASSIC PTC formed of Papillae with fibrovascular core and nuclear feature of PTC.
(B) Immunohistochemical examination revealed strong membranous expression of CD73(green arrow: refer to strong membranous expression.
(C) Strong cytoplasmic expression of CK19 (black arrow: refer to strong cytoplasmic expression).



4): Follicular variant papillary thyroid carcinoma

(A) Histopathological examination showed follicular variant of PTC that showed follicular epithelial cells with prominent nuclear clearing arranged into follicles (H&Ex400).

(B) Immunohistochemical examination showed strong cytoplasmic positivity of CK19 (orange arrow: refer to strong cytolasmic expression).

(C) Moderate cytoplasmic positivity of CD73 (blue arrow: refer to moderate cytoplasmic expression).

DISCUSSION

According to the national population-based cancer registry programme, thyroid cancer is the sixth most prevalent tumor in females in Egypt, accounting for 3.28% of all cancer cases. In men, it represents 0.95% of total cancer cases [13].

Based on the most recent registry from the Egyptian National Cancer Institute (NCI), primary malignant thyroid neoplasms accounted for 1.97% of all malignant neoplasms at NCI and made up 74.7% of malignant endocrine tumors. Based on the latest registry data, PTC accounts for 70.94% of all primary malignant thyroid tumors [14].

The PTC accounts for just 1% of all malignancies and comprises 70–80% of all thyroid cancers. It is associated with the most favorable overall prognosis. The formation of this neoplasm is linked to various causes, including genetic mutations, growth factors, and exposure to radiation [15]. The PTC is a type of cancer that originates from the cells lining the thyroid gland and has characteristics of follicular cell differentiation, along with a specific set of nuclear markers. Approximately 10% of individuals may exhibit metastatic disease upon their initial presentation. The prognosis is generally favorable for the majority of patients, particularly those under the age of 45 [16].

The PTC is identified through the examination of both cytological and histological samples, which reveal certain changes in the nucleus. These changes include the elongation of the nucleus, the clearing of chromatin, the presence of grooves within the nucleus, and the presence of inclusions [17]. Due to the overlapping histopathologic characteristics of papillary thyroid carcinoma (PTC) with other benign and non-neoplastic lesions. The purpose of this study was to assess the diagnostic accuracy of two immunohistochemistry markers, CD73 and CK19, both individually and in combination, for distinguishing PTC from other neoplastic and non-neoplastic mimickers. Several studies have utilized immunohistochemical markers to aid in distinguishing between PTC and other

similar conditions, whether they are neoplastic or non-neoplastic. One such marker that has been utilized is galectin III, HBME-1 [18], CK19 [19], TROP2 [20], and others.

The cases were chosen based on the histological examination, as the histopathological criteria were deemed a reliable standard for assessing the diagnostic efficacy of the markers being examined. Several investigations have shown that CK19 staining is absent in benign thyroid lesions, however, other research has found a variable range of 20 to 75% positive staining, particularly in the follicular version of these lesions [11].

In this study, CK19 was shown to be positive in all cases of papillary thyroid carcinoma (PTC) and 66.7% of suspicious cases. There were substantial differences between these two groups. CK19 demonstrated a sensitivity of 100% and a specificity of 33.3% in diagnosing PTC. Expression was poor in intensity for all stained suspicious cases, but 53 (88.3%) of PTC cases exhibited strong intensity. Consistent with our discovery in the Bose et al. study, all instances of papillary thyroid carcinoma (PTC) exhibited diffuse and robust expression of CK19. Immunoreactivity to CK19 was seen in 50% of MNG and 75% of FA. Expression was the central focus and had a low level of intensity in all of these instances [21].

In addition, the research conducted by Nasr et al. observed a significant prevalence of CK19 positive in benign lesions, reaching 68%. However, the staining intensity in these benign lesions was found to be modest [22]. Miettinen et al. have verified that CK19 is a valuable indicator for distinguishing between papillary cancer and papillary hyperplasia [23]. Cheung et al. found that 80% of papillary thyroid carcinomas (PTCs) and 57% of follicular variant papillary thyroid carcinomas (FVPTCs) had diffuse and moderate to strong staining of CK19 [24]. Based on the findings of Guyétant et al., the accuracy of CK19 as a diagnostic marker for papillary carcinomas was determined to be 100% for sensitivity and 82.5% for specificity [25]. Alshenawy demonstrated that the sensitivity and specificity of ck19 to differentiate between PTC and suspicious lesions were 65% and 78% respectively [11].

We found comparable results in the literature as regards the ability of CK19 to differentiate PTC from another benign thyroid lesion. The study conducted by Isic Dencic et al. revealed that classical papillary thyroid cancer exhibited an 88% positivity rate, however, its follicular variant counterpart demonstrated a lower positivity rate of just 65% [26]. Also, in the Nechifor-Boilă et al., study, (83%) of classical papillary thyroid carcinoma showed positivity, while (100%) of follicular variants of papillary thyroid carcinomas were negative [27]. One possible reason for this discrepancy in staining could be attributed to the genetic profile of each type of papillary thyroid cancer [28].

The BRAF ^{V600E} mutation is the predominant genetic alteration in classical papillary thyroid cancer, occurring in 45-80% of cases [29]. Unlike the study of Wa Kammal et al., we find that CK19 staining could differentiate the PTC variant [30]. Isic Dencic et al., indicate that CK19 may carry a prognostic impact, as they find the correlation between Ck19 and the TNM stage [26]. While in our study we didn't find any correlation between Ck19 and LN status, similar to the finding of [30].

There has been very little research examining how CD73 expression affects the clinicopathologic outcomes of patients with thyroid tumors. A recent study found that increased levels of CD73 mRNA were correlated with bigger tumor growth and lymph node metastasis. However, the analysis of CD73 protein expression using immunohistochemistry did not show any statistically significant results [31].

In the present study, CD73 was positive in 95% of PTC cases and 58.3% of suspicious cases with significant differences between both groups, CD73 showed 95% sensitivity and 41.7% specificity in of diagnosis PTC. In all stained suspicious cases, expression was weak/moderate intensity unlike PTC cases showed moderate/strong intensity at 65%.

In the study of Monteiro et al., the vast majority (98%) of PTC cases express CD73 and 60% showed moderate/ strong staining intensity [12]. The prevailing consensus is that the process of dedifferentiation of differentiated thyroid carcinomas is the typical pathway for the development of carcinomas. Due to the variability in CD73 expression across these carcinomas, it is possible that tumours with higher H-scores originated from papillary thyroid carcinoma (PTC), while tumors that are negative or weakly positive may have originated from other types of cancer [33]. Similar to the results of Monteiro et al., we didn't find a correlation between CD73 expression and nodal status [12]. But we agree with the literature that strongly stained CD73 cases are associated with lymphatic, necrosis and an increase in the size of the tumor [32].

The combination of both markers showed 100% sensitivity, 16.7% specificity, 85.7% positive predictive value, 100% negative predictive value, and 86.1% accuracy. Lowest specificity because negative cases with CD73 were positive with Ck19. Finally, CK19 and CD73 have high expression in PTC and promising results to differentiate PTC from benign lesions.

CONCLUSION

Our study demonstrated that Cytokeratin 19 is a potentially useful marker in differentiating malignant

thyroid tumors especially papillary thyroid carcinomas, from benign thyroid condition.

A strong and diffusely positive Cytokeratin 19 staining strongly supports malignancy, particularly when papillary thyroid carcinoma is suspected. However, the Cytokeratin 19 immunohistochemical staining is not helpful in the cases of follicular variant of papillary thyroid carcinoma. On the other hand, negative or weakly positive Cytokeratin 19 staining suggests a benign condition, provided the morphology supports it.

CD73 is highly expressed in PTC, presenting a distinct IHC pattern, explaining that tumors with higher H-scores potentially developed from PTC, while negative or faintly positive tumors could have developed from other forms. We could say that Ck19 or the combination of both markers could provide the best sensitivity, while CD73 provides the best specificity at 41%.

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REFERENCES

1. **Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al.** American Thyroid Association Management Guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid. 2016;26(1):1-133.
2. **Krajewska J, Kukulska A, Oczko-Wojciechowska M, Kotecka-Blicharz A, Drosik-Rutowicz K, Haras-Gil M, et al.** Early diagnosis of low-risk papillary thyroid cancer results rather in overtreatment than better survival. Front Endocrinol (Lausanne). 2020;11:782.
3. **Sutherland R, Tsang V, Clifton-Bligh RJ, and Gild M.** Papillary thyroid microcarcinoma: Is active surveillance always enough? Clin Endocrinol (Oxf) . 2021;95(6):811-817.
4. **Agarwal S, Bychkov A, and Jung C.** Emerging biomarkers in thyroid practice and research. Cancers (Basel). 2021 Dec 31;14(1):204.
5. **Selves J, Long-Mira E, Mathieu M, Rochaix P, and Ilié M.** Immunohistochemistry for diagnosis of metastatic carcinomas of unknown primary site. Cancers (Basel). 2018 Apr 5;10(4):108.
6. **Whiteside T.** Targeting adenosine in cancer immunotherapy: a review of recent progress. Expert Rev Anticancer Ther. 2017;17(6):527-535.
7. **Kabbash M, Abdallah H, El Shenawy A, and Mohamed M.** The prevalence of thyroid cancer in patients with multinodular ggoiter. Egypt J Hosp Med. 2019;77(6):5906-5910.
8. **Jung C, Bychkov A, and Kakudo K.** Update from the 2022 World Health Organization Classification of Thyroid Tumors: A Standardized Diagnostic Approach. Endocrinol Metab. 2022;37(5):703-718.
9. **Tuttle R, Haugen B, and Perrier N.** Updated American Joint Committee on Cancer/Tumor-Node-Metastasis Staging System for Differentiated and Anaplastic Thyroid Cancer (Eighth Edition): What Changed and Why? Thyroid. 2017;27(6):751.
10. **Hawes D, Shi S, Dabbs D, Taylor C, and Cote R.** Immunohistochemistry. Mod Surg Pathol. 2009;1:48.
11. **Alshenawy H.** Utility of immunohistochemical markers in differential diagnosis of follicular cell-derived thyroid lesions. J Microsc Ultrastruct. 2014; 2(3):127.
12. **Monteiro I, Missiaglia E, Sciarra A, Santos JV, Bouilly J, Romero P, et al.** CD73 expression in normal, hyperplastic, and neoplastic thyroid: a systematic evaluation revealing CD73 overexpression as a feature of papillary carcinomas. Virchows Arch. 2021;479(1):209-214.
13. **1Ibrahim A, Khaled H, Mikhail N, Baraka H, and Kamel H.** Cancer incidence in Egypt: Results of the national Population-Based Cancer Registry Program. J Cancer Epidemiol. 2014;2014:437971.
14. **Abdou A, Shabaan M, Abdallha R, and Nabil N.** Diagnostic value of TROP-2 and CK19 expression in papillary thyroid carcinoma in both surgical and cytological specimens. Clin Pathol. 2019 Jul 22;12:2632010X19863047.
15. **Erdem H, Gündogdu Cemal C, and Üipal S.** Correlation of E-cadherin, VEGF, COX-2 expression to prognostic parameters in papillary thyroid carcinoma. Exp Mol Pathol. 2011;90(3):312-317.
16. **Limaiem F, Rehman A, Anastasopoulou C, and Mazzoni T.** Papillary thyroid carcinoma. StatPearls. Published online January 1, 2023. Available at https://www.ncbi.nlm.nih.gov/books/NBK536943/ Accessed July 2, 2023.
17. **Ashwini B, Nirmala C, Natarajan M, and Biligi D.** A study to evaluate association of nuclear grooving in be0nign thyroid lesions with RET/PTC1 and RET/PTC3 gene translocation. Thyroid Res. 2023 Jul 3;16(1):21.
18. **Dunđerović D, Lipkovski JM, Boričic I, Soldatović I, Božic V, Cvejić D, et al.** Defining the value of CD56, CK19, Galectin 3 and HBME-1 in diagnosis of follicular cell derived lesions of thyroid with systematic review of literature. Diagn Pathol. 2015;10(1):1-18.
19. **Abouhashem N and Talaat S.** Diagnostic utility of CK19 and CD56 in the differentiation of thyroid papillary carcinoma from its mimics. Pathol Res Pract. 2017;213(5):509-517.
20. **Bychkov A, Sampatanukul P, Shuangshoti S, and Keelawat S.** TROP-2 immunohistochemistry: a

highly accurate method in the differential diagnosis of papillary thyroid carcinoma. Pathology. 2016;48(5):425-433.

21. **Bose D, Das R, Chatterjee U, and Banerjee U.** Cytokeratin 19 immunoreactivity in the diagnosis of papillary thyroid carcinoma. Indian J Med Paediatr Oncol. 2012;33(2):107.
22. **Nasr M, Mukhopadhyay S, Zhang S, and Katzenstein A.** Immunohistochemical markers in HBME1 combined with CK19 immunostaining. Mod Pathol. 2006;19(12):1631-1637.
23. **Miettinen M, Kovatich AJ, and Kärkkäinen P.** Keratin subsets in papillary and follicular thyroid lesions. A paraffin section analysis with diagnostic implications. Virchows Arch. 1997;431(6):407-413.
24. **Cheung C, Ezzat S, Freeman J, Rosen I, and Asa S.** Immunohistochemical diagnosis of papillary thyroid carcinoma. Mod Pathol. 2001;14(4):338-342.
25. **Guyétant S, Michalak S, Valo I, and Saint-André J.** Diagnosis of the follicular variant of papillary thyroid carcinoma. Significance of immunohistochemistry. Ann Pathol. 2003;23(1):11-20.
26. **Isic Dencic T, Cvejic D, Paunovic I, Tatic S, Havelka M, and Savin S.** Cytokeratin19 expression discriminates papillary thyroid carcinoma from other thyroid lesions and predicts its aggressive behavior. Med Oncol. 2013 Mar;30(1):362.
27. **Nechifor-Boilă A, Cătană R, Loghin A, Radu T, and Borda A.** Diagnostic value of HBME-1, CD56, Galectin-3 and Cytokeratin-19 in papillary thyroid carcinomas and thyroid tumors of uncertain malignant potential. Rom J Morphol Embryol. 2014;55(1):49-56.
28. **Suh Y, Moon H, Choe J, and Park H.** The cancer genome Atlas validation of ancillary tests for classifying papillary thyroid carcinoma. Int J Thyroidol. 2017;10(1):24-35.
29. **Basolo F, Macerola E, Poma A, and Torregrossa L.** The 5th edition of WHO classification of tumors of endocrine organs: changes in the diagnosis of follicular-derived thyroid carcinoma. Endocrine. 2023; 80(3):470.
30. **Wa Kammal WS, Yahaya A, Shah SA, Abdullah Suhaimi SN, Mahasin M, Mustangin M, et al.** The diagnostic utility of cytokeratin 19 in differentiating malignant from benign thyroid lesions. Malays J Pathol. 2019;41(3):293-301.
31. **Jeong YM, Cho H, Kim TM, Kim Y, Jeon S, Bychkov A, et al.** CD73 Overexpression Promotes Progression and Recurrence of Papillary Thyroid Carcinoma. Cancers (Basel). 2020;12(10).
32. **Bertoni APS, Bracco PA, de Campos RP, Lutz BS, Assis-Brasil BM, Meyer ELS, et al.** Activity of ecto-5'-nucleotidase (NT5E/CD73) is increased in papillary thyroid carcinoma and its expression is associated with metastatic lymph nodes. Mol Cell Endocrinol. 2019;479:54-60.
33. **Kakudo K, Bychkov A, Bai Y, Li Y, Liu Z, and Jung C.** The new 4th edition World Health Organization classification for thyroid tumors, Asian perspectives. Pathol Int. 2018;68(12):641-664.

الملخص العربي

الدور التشخيصي للصبغات المناعية سي . ك 19 و سي . د ٧٣ في سرطان الغدة الدرقية اللحيمي

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ملخص البحث

الخلفية: هناك شك فى تشخيص بعض آفات الغدة الدرقية على نطاق واسع، حتى بين علماء الأمراض ذوي الخبرة الكبيرة. وهذا صحيح خصوصا في حالات سرطان الغدة الدرقية الحليمي، حيث يمكن أن تكون الخصائص النووية غير واضحة.في الآونة الأخيرة، وقد تم استخدام العديد من الاختلافات الجزيئية في سرطان الغدة الدرقية للتمييز بين أورام الغدة الدرقية الخبيثة والحميدة. كما تم استخدام المؤشرات الحيوية (سى . ك ١٩) و (سى .د ٧٣) بنجاح في الممارسة السريرية، مما أدى إلى تحسن كبير في تشخيص سرطان الغدة الدرقية قبل الجراحة.

الهدف: تقييم دور سى . ك ١٩ و سى . د ٧٣ في تشخيص سرطان الغدة الدرقية اللحيمي.

الطرق: أجريت هذه الدراسة بأثر رجعي في مستشفى جامعة الأزهردمياط الجديدة، ومستشفى الزهراء الجامعى، القاهرة. شملت الحالات التي تمت دراستها ستون حالة سرطان الغدة الدرقية الحليمي واثنتي عشرة حالة غير ورمية. تم تقييم وجود النشاط المناعي في كل علامة وسجل على أنه سلبي إذا لم يكن هناك صبغه أو صبغه ضعيف في أقل من ١٠٪ من الخلايا. تم تسجيل أي نشاط مناعي آخر على أنه إيجابي.

النتائج: كان لـ (سى . ك ١٩) حساسية أعلى ولكن أقل خصوصية من (سى . د ٧٣)، بينما كان لاستخدام الصبغتين معا خصوصية أقل منه (سى .ك ١٩) وحده وحساسية ١٠٠%

الإستنتاج: يمكننا القول أن (سى . ك ١٩) أو مزيج من كلا الصبغتين المناعيتين يمكن أن يوفرا أفضل حساسية، في حين يوفر(سى.د ٧٣) أفضل خصوصية بنسبة ٤١٪.

الكلمات المفتاحية: سرطان الغدة الدرقية اللحيمي، سى . ك ١٩؛ سى. د ٧٣، صبغات مناعية.

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