Article published online: 2026-01-15

Study of PD-L1 Expression in Papillary Thyroid Carcinoma and Its Correlation to the Clinicopathologic Characteristics

Asmaa Gamal Mohamed El Sayed[1] Dina Ragab Diab Ibrahim[1] Mahmoud Mahmoud El-Leithy[1] Mai Mohamed Ali Ezz El Din[1] Hoda Hassan Abou Gabal[2] Reham Mohamed Faheim[1]

[1] Department of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt
[2] Department of Pathology, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Address for correspondence Asmaa Gamal Mohamed El Sayed, MSc, Department of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Ain Shams University, Cairo 1181, Egypt (e-mail: asmaagamal@med.asu.edu.eg).

Ind J Med Paediatr Oncol

Abstract

Introduction Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer, generally associated with a favorable prognosis. Programmed death-ligand 1 (PD-L1), an immune checkpoint protein, has been implicated in tumor immune evasion and is emerging as a potential prognostic marker in PTC.

Objectives The study aimed to assess PD-L1 expression in patients with PTC and also to determine its correlation with clinicopathologic parameters.

Materials and Methods This is a cross-sectional study conducted to assess the PD-L1 status by immunohistochemistry on formalin-fixed and paraffin-embedded surgical tissues of 50 patients diagnosed with PTC and its variants in the period from 2020 to 2022. The clinicopathologic features were studied and correlated with the PD-L1 status.

Results PD-L1–positive expression was detected in 16/50 patients (32%) at a 1% threshold. In our study, a statistically significant correlation was found between patients with PD-L1–positive tumor cells and higher T stage ($p = 0.021$), and positive pathological lymph nodes (LNs) ($p = 0.01$). All the 16 patients who were found to have PD-L1–positive expression received radioactive iodine treatment ($p = 0.034$), whereas no association was found with age ($p = 0.197$), sex ($p = 0.584$), multifocality ($p = 0.566$), lymphovascular invasion ($p = 0.061$), extrathyroid extension ($p = 0.725$), thyroiditis ($p = 0.135$), histological variants ($p = 0.520$), margins ($p = 0.410$), and postoperative thyroglobulin ($p = 0.120$).

Conclusion PD-L1 expression correlates with T stage and pathological LNs and may be used as a prognostic marker for patients with PTC. Further follow-up needs to be done to confirm the prognostic value of PD-L1 expression in PTC.

Keywords
- PD-L1 expression
- papillary thyroid carcinoma
- radioactive iodine
- thyroidectomy
- prognostic marker

DOI https://doi.org/10.1055/s-0045-1815718.
ISSN 0971-5851.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Introduction

Thyroid cancer is the most common endocrine malignancy, accounting for 2.1% of all new malignancies (excluding skin cancer and in situ carcinomas) diagnosed annually worldwide.[1] According to Global Cancer Observatory (IARC) data in 2020, an estimated 586,000 persons per year are diagnosed with thyroid cancer, with incidence ranking ninth among all cancer diagnoses.[2] Papillary thyroid carcinoma (PTC) is the most common histologic subtype of thyroid carcinoma, accounting for 90% of new cases, and has the best prognosis.[3]

Programmed death 1 (PD-1) is a cell surface protein expressed on many immune cells, and its main ligand is programmed death-ligand 1 (PD-L1), which is normally expressed on macrophages and several epithelial cells.[4] In recent years, immunocheckpoint blocking therapy targeting the PD-1/PD-L1 axis has achieved good results in a variety of malignant tumors, pushing tumor immunotherapy to a new milestone.[5]

Chowdhury et al[6] and Angell et al[7] studies showed that PD-L1–positive expression in PTC correlates with a greater risk of recurrence and shortened disease-free survival, supporting its potential application as a prognostic marker for PTC.[8]

The study aimed to assess PD-L1 expression in patients with PTC and its variants and also to determine its correlation with clinicopathologic parameters.

Materials and Methods

Patients

The study was a cross-sectional study conducted on 50 patients diagnosed with PTC presented at the Head and Neck Unit, Department of Clinical Oncology and Nuclear Medicine, Ain Shams University Hospitals in the period from 2020 to 2022.

Each patient included in the research was labeled anonymously and given a new serial number to respect the patients' privacy. Written informed consent was obtained from all patients prior to study inclusion. All procedures performed in the current study were approved by the Ethics Committee at the Faculty of Medicine, Ain Shams University (FMASU MD 37/2021). Patients were selected according to the inclusion/exclusion criteria. Sampling method was convenience sampling (all eligible patients in the previously determined period fulfilling the eligibility criteria were included).

The inclusion criteria were as follows: (1) patients aged 18 years or older, (2) pathologically confirmed PTC and its variants, (3) who underwent surgery in the form of total thyroidectomy or subtotal thyroidectomy, and (4) all tumor stages. Patients who had microcarcinoma and inadequate or insufficient tissue samples were excluded.

Clinical Data

The archived files of the patients were studied for age, sex, and comorbidities, operative details (maximal tumor size, nodal status, tumor histology, multifocality, lymphovascular invasion [LVI], extrathyroid extension [ETE], thyroiditis, and resection margin status), postoperative thyroglobulin (Tg), and radioactive iodine (RAI) treatment.

Each Block Is Subjected To

Hematoxylin and eosin stained slides preparation, which were re-examined for confirming the diagnosis according to the 2022 World Health Organization classification and re-evaluation of other histologic parameters. Staging was performed based on the AJCC UICC 8th edition (2017).[9] Paraffin-embedded full tissue sections of 4-µm thickness were prepared on positively charged slides for immunohistochemical staining.

Immunohistochemical Staining

For immunohistochemical staining, the Dako Autostainer Link 48 autostainer (Dako/Agilent Technologies) was used. Antigen retrieval was performed using PT Link with EnVision FLEX Target Retrieval Solution (low pH; Dako/Agilent Technologies) (►**Figs. 1** and **2**).

Primary Antibody

The primary antibody was performed using monoclonal mouse anti-human PD-L1 (clone 22C3 from Dako company; catalog number: 156-B7-100), diluted at 1:150. The primary antibody was incubated with the pretreated tissue sections for 30 minutes at room temperature. The EnVisionTM FLEX HRP visualization system was used. Primary antibodies were used against DAB as a chromogen and hematoxylin as a counterstain. When the staining run was complete, the slides were moved from the instrument, washed well with absolute alcohol followed by xylene, and coverslipped. Positive and negative controls should be run simultaneously with patient specimens.

Other reagents used were xylene, ethanol, absolute alcohol, distilled water, reaction buffer, EZ prep, and LCS.

Control Slides

Positive Control

Tonsil tissue sections were used as positive controls.

Negative Control

Negative control slides used were papillary thyroid tissue. Sections from the same tissues were processed in the same immunostaining procedure with the omission of the primary antibody.

Immunohistochemical Analysis

PD-L1 positivity was assessed using the tumor proportion score (TPS). Cytoplasmic positivity is disregarded. Cutoff value for PD-L1 positivity was defined as $\geq$ 1% staining of tumor cells, and strong positivity was defined as $>$ 50%.

Statistical Methods

Descriptive statistics were utilized to present the data, including frequencies and percentages for qualitative variables, and means and standard deviations (SDs) for

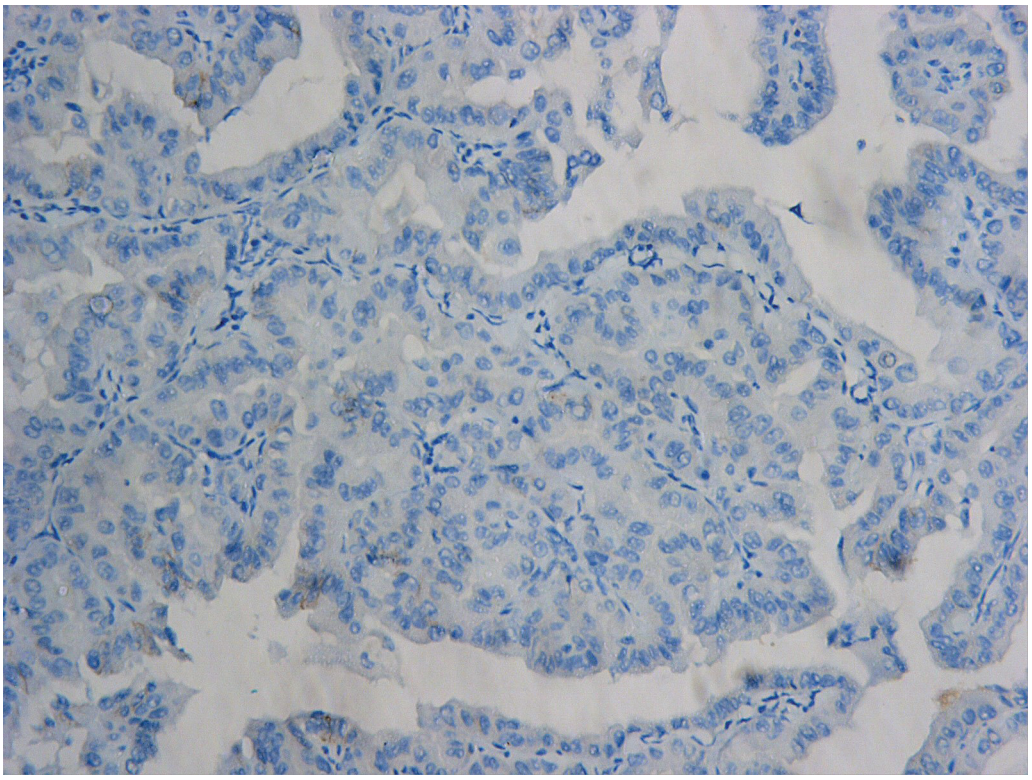

Fig. 1 A case of classic PTC showing negative PD-L1 expression (IHC ×200). IHC, immunohistochemistry; PD-L1, programmed death-ligand 1; PTC, papillary thyroid carcinoma.

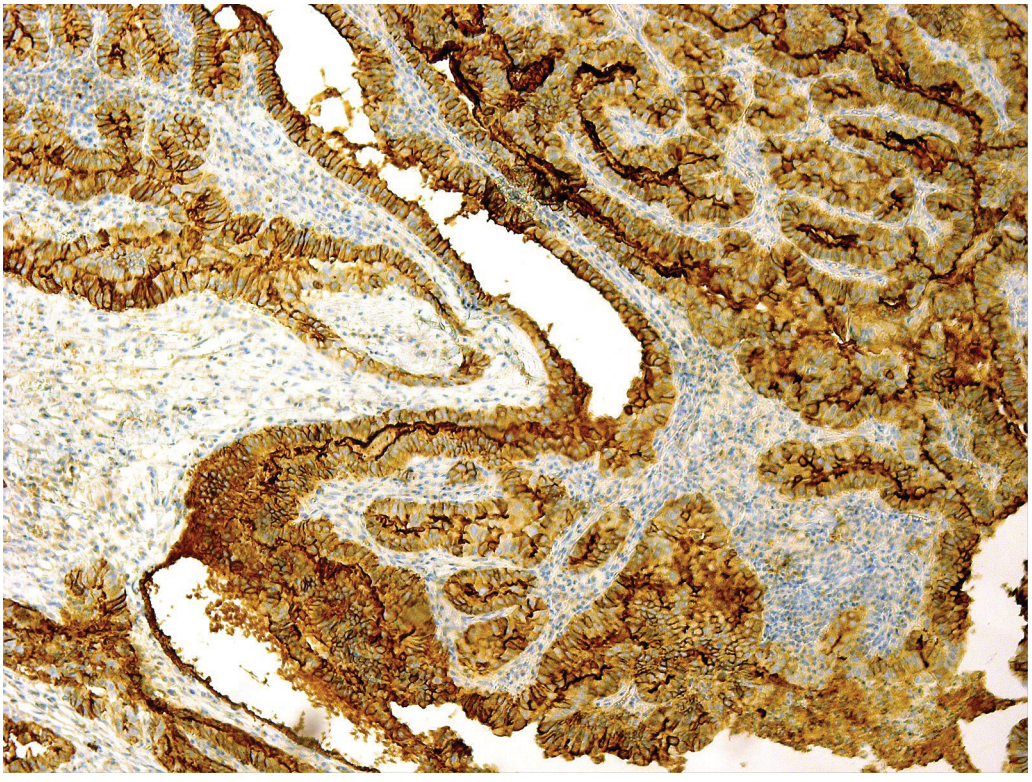

Fig. 2 A case of tall cell variant of PTC showing diffuse PD-L1 membranous expression (IHC ×100). IHC, immunohistochemistry; PD-L1, programmed death-ligand 1; PTC, papillary thyroid carcinoma.

quantitative variables. The comparison of qualitative variables was conducted using the chi-square test. In cases where the expected values in any of the cells within a 2×2 table were less than 5, Fisher's exact test was employed instead. For larger cross-tables exceeding 2×2, the Monte Carlo test was used when the expected value in two or more cells was less than 5. Statistical significance was determined at a *p*-value threshold of < 0.05.

Ethical Approval

All procedures performed in the current study were done in accordance with the Helsinki Declaration and the study is approved by the Ethics Committee at the Faculty of Medicine, Ain Shams University (FMASU MD 37/2021).

Results

Patients' Characteristics

This study included 50 patients with tissue diagnosis of PTC who presented to the Department of Clinical Oncology Department, Ain Shams University from January 2020 to December 2022. The age in the study population ranged from 20 to 75 years; the mean age at diagnosis was 43 years (SD = 13.11). The clinicopathologic characteristics and the received treatment of the 50 patients are presented in ►**Tables 1** and **2**.

Table 1 Patients characteristics ($n = 50$)

Variable	*N*	%
Age (y)		
< 55	42	84
≥ 55	8	16
Gender		
Male	4	8
Female	46	92
Diabetes mellitus		
No	46	92
Yes	4	8
Hypertension		
No	45	90
Yes	5	10
Other comorbidities		
No	46	92
Yes	4	8
Size		
1–2 cm	20	40
> 2–4 cm	21	42
> 4 cm	9	18
Pathological TNM		
T		
1	18	36
2	18	36
3	14	28
4	0	0
N		
N0	38	76
N1	12	24
M		
M0	50	100
M1	0	0
TNM stage eighth		
I	46	92
II	4	8
III	0	0
IV	0	0
Multifocal		
No	31	62
Yes	19	38
LVI		
No	34	68
Yes	16	32
ETE		
No	39	78
Yes	11	22
Thyroiditis		
No	37	74
Yes	13	26
Histology		
Classical papillary	33	66
Follicular variant	9	18
Other variants	8	16
Mixed classical papillary and follicular	3	6
Tall	1	2
Oncocytic	3	6
Solid cell	1	2
Margins		
Negative	38	76
Positive	12	24
Postoperative Tg		
< 1	16	32
1–10	21	42
> 10	10	20
N/A	3	6

Abbreviations: ETE, extrathyroid extension; LVI, lymphovascular invasion; N/A, not available; Tg, thyroglobulin.

Table 2 Treatment of the study population ($n = 50$)

Variable	*N*	%
Type of surgery		
Total thyroidectomy	50	100
Lobectomy	0	0
LND		
Yes	21	42
No	29	58
RAI treatment		
Yes	42	84
No	8	16
Aim of RAI treatment		
Remnant ablation	4	9.5
Adjuvant treatment	38	90.5
Macroscopic residual or metastatic	0	0

Abbreviations: LND, lymph node dissection; RAI, radioactive iodine.

T3 according to AJCC UICC 8th edition (2017) is defined as tumor size > 4 cm, or gross ETE; therefore, there is a discrepancy between the number of patients with regard to tumor size and T stage. Regarding lymph node (LN) status, 21 patients underwent lymph node dissection (LND), with 12 patients found to have pathological LNs.

Immunohistochemistry Results

PD-L1 was detected by immunohistochemistry (IHC) in tumor cells; PD-L1 was positive in tumor cells for 16 patients (32%) at a 1% threshold, while 34 patients (68%) had negative PD-L1 in tumor cells, with 18.8% found to have a strong positivity of > 50%.

The clinicopathologic characteristics of 50 patients according to tumoral PD-L1 status are presented in ►**Table 3**. In correlation with clinical and pathological factors, patients with PD-L1–positive tumor cells had a higher T stage ($p = 0.021$), with 66.7% having tumor size > 4 cm ($p = 0.000$) and positive pathological LNs ($p = 0.003$). A total of 16 out of 50 patients were found to have PD-L1 positive, and all of them received RAI ($p = 0.034$). Patients

Table 3 Relation between clinicopathologic data of studied sample and PD-L1 status

Variable	PD-L1				*p*-Value
	Negative		Positive		
	N	%	*N*	%	
Age (y)					
< 55	27	64.3	15	35.7	0.197
≥ 55	7	87.5	1	12.5	
Gender					
Male	2	50	2	50	0.584
Female	32	69.6	14	30.4	
Size					
1–2 cm	18	90	2	10	0.000
> 2–4 cm	13	61.9	8	38.1	
> 4 cm	3	33.3	6	66.7	
T					
1	16	88.9	2	11.1	0.021
2	12	66.7	6	33.3	
3	6	42.9	8	57.1	
4	–	–	–	–	
N					
N0	30	88.9	8	11.1	0.003
N1	4	33.3	8	66.7	
M					
M0	34	68	16	32	–
M1	–	–	–	–	–

(*Continued*)

Table 3 (*Continued*)

Variable	PD-L1				*p*-Value
	Negative		Positive		
	N	%	*N*	%	
Stage					
I	31	67.4	15	32.6	1.000
II	3	75	1	25	
III	0	0	0	0	
IV	0	0	0	0	
Multifocal					
No	22	71	9	29	0.566
Yes	12	63.2	7	36.8	
LVI					
No	26	76.5	8	23.5	0.061
Yes	8	50	8	50	
ETE					
No	27	69.2	12	30.8	0.725
Yes	7	63.6	4	36.4	
Thyroiditis					
No	23	62.2	14	37.8	0.135
Yes	11	84.6	2	15.4	
Histology					
Classical papillary	23	69.7	10	30.3	0.520
Follicular variant	7	77.8	2	22.2	
Other variants	4	50	4	50	
Margins					
Negative	27	71.1	11	28.9	0.410
Positive	7	58.3	5	41.7	
Postop Tg					
< 1	14	87.5	2	12.5	0.120
1–10	12	57.1	9	42.9	
> 10	7	70	3	30	
N/A	1	33.3	2	66.7	
RAI					
No	8	100	0	0	0.034
Yes	26	61.9	16	38.1	

Abbreviations: ETE, extrathyroid extension; LVI, lymphovascular invasion; N/A, not available; PD-L1, programmed death-ligand 1; RAI, radioactive iodine; Tg, thyroglobulin.

with PD-L1–positive tumor cells had a trend toward increased risk for recurrence but not statistically significant ($p = 0.190$).

Regarding LVI, there was a trend toward correlation with PD-L1 positivity but did not reach statistically significant correlation ($p = 0.061$). There was no significant association between PD-L1 status and age, sex, stage, initial metastasis, multifocality, ETE, thyroiditis, histological variants, margins, and postoperative Tg.

Discussion

PTC is the most common histologic subtype of thyroid cancer, accounting for 90% of new cases, and has the best prognosis.[3]

We studied 50 patients with PTC who presented to the Department of Clinical Oncology, Ain Shams University from January 2020 to December 2022. We assessed PD-L1 expression and correlation to the clinicopathologic characteristics.

In our study, female patients were ~92% which represent the majority of the study population, and this agrees with many studies that showed a female predominance in PTC.[10,11]

With regard to the TNM staging, the study showed a predominance of stage I in ~92%, which goes with many studies that recorded predominance of stage I, which is due to improvements in radiologic screening at an early stage.[12–14]

The expression of PD-L1 on tumor cells has been studied as a possible predictive biomarker in anti-PD-L1-directed cancer immunotherapy.[5]

Chowdhury et al[6] and Angell et al[7] showed that PD-L1–positive expression in PTC correlates with a greater risk of recurrence and shortened disease-free survival, supporting its potential application as a prognostic marker for PTC.

Immune checkpoint inhibitor therapies targeting CTLA4 and the PD1–PD-L1 axis have been tested in patients with advanced thyroid cancers. In the KEYNOTE-028 trial, 22 patients with positive PD-L1 ($\geq$ 1% of the tumor was PD-L1 positive) advanced RAI refractory differentiated thyroid carcinoma (including papillary and follicular thyroid carcinomas) were treated with pembrolizumab for up to 2 years. Median progression-free survival was 7 months (95% confidence interval [CI] 2–14 months), and median overall survival was not reached (95% CI, 22 months to not reached).[15] In the KEYNOTE-158 study, the Food and Drug Administration approved pembrolizumab as a treatment option for patients with tumor mutational burden –high RAI-refractory PTC.[16]

Of clinical relevance, PD-L1 overexpression appears to predict worse prognosis, and identifying thyroid cancer patients at risk of tumor progression, representing real hope for the early management of advanced well-differentiated thyroid cancer.[17]

PD-L1 positivity was assessed using TPS instead of combined positive score to avoid the influence of lymphocytes, which can raise PD-L1 positivity in thyroid cancer patients with lymphocytic thyroiditis. In a prior study conducted by Fadia et al, PD-L1 positivity was shown to be considerably higher in PTCs with lymphocytic thyroiditis (39.1%) than in PTCs without lymphocytic thyroiditis (6.1%).[18] The same results were also reported by a meta-analysis conducted by Girolami et al.[4]

PD-L1 positivity in tumor cells was recorded for 16 patients (32%) at a 1% threshold using 22C3 in our study. Studies that investigated PD-L1 expression by IHC have reported positivity rates ranging from 6 to 82.5% for tumor cells at the same cutoff. However, different antibodies were used (clone E1L3N, ab82059, and SP142).[6,8]

Another study evaluating PD-L1 in patients with thyroid carcinoma, which used the same clone as our study (22C3), demonstrated that PD-L1 was positive in 15% of patients with less aggressive types of thyroid carcinoma.[19] Also, the KEYNOTE-028 trial, which assessed the antitumor activity of anti-PD-1 pembrolizumab in advanced thyroid cancer, used the 22C3 clone.[15]

In the present study, there was no significant association between PD-L1 status and age, sex, stage, initial metastasis, multifocality, margins, LVI, and ETE. These findings are in concordance with other studies that assessed the same clinicopathologic parameters. As reported by Ahn et al and Bai et al, no significant correlation was found between PDL-1 positivity and these features.[8,12]

A meta-analysis conducted by Wan et al found that higher expression of PD-L1 in patients with thyroid cancer was associated with tumor size $\geq$ 2 cm.[20] Our study showed that there is statistically significant correlation between PD-L1 positivity and larger tumor size $>$ 4 cm ($p = 0.021$), where 66.7% of patients with positive PD-L1 had tumor size $>$ 4 cm ($p = 0.000$).

Our study reported no significant correlation between PD-L1 and thyroiditis ($p = 0.135$). This is inconsistent with the results of a meta-analysis conducted by Girolami et al.[4] This may be due to the assessment of PD-L1 by TPS in our study.

According to a study conducted by Chowdhury et al, PD-L1–positive expression in PTC correlates with aggressive subtypes of PTC ($p = 0.001$).[6] This is agreed by Wittmann et al,[21] that there is a significant correlation between aggressive subtypes of PTC and PD-L1 positivity ($p = 0.0274$). In our study, there was no significant correlation between the histological subtypes of PTCs and PD-L1 expression ($p = 0.520$).

In our study population, 42% of patients underwent LND, 24% of them had LN metastasis. Our results showed a significant correlation with positive PD-L1 expression ($p = 0.01$). This is agreed by An et al[11] that PD-L1–positive expression was closely associated with metastatic LNs ($p = 0.036$). Also, a study conducted by Neamah and Janabi showed that there is a significant correlation between PD-L1 status and pathological LNs ($p = 0.0001$).[22]

In the present study, 16 out of 50 patients were found to have positive PD-L1 expression, all of them received RAI ($p = 0.034$). This may be due to a significant correlation with some adverse clinicopathologic features, such as tumor size and LN metastasis.

To the best of our knowledge, this is the first study to assess PD-L1 in PTC in the Egyptian population, using the 22C3 clone, the same clone used by the KEYNOTE-028 trial for using pembrolizumab in advanced thyroid cancer, with correlation to adverse clinicopathologic parameters.

We acknowledge some limitations in the present study that should be considered when interpreting our findings. The sample size ($N = 50$) is relatively small, which limits the statistical power and necessitates caution in interpreting nonsignificant p-values. Furthermore, there is a low representation of advanced cases (including metastatic disease) and an absence of long-term follow-up data. These limitations are largely due to the retrospective, single-center nature of the study, and the availability of archived tissue blocks. Despite these significant limitations, the fact that we found statistically significant correlations between PD-L1 expression and major indicators of aggressive disease (T stage, $p = 0.021$; nodal status, $p = 0.01$) suggests a robust biological association.

In the last decade, we have witnessed the revolution of immunotherapy as a true “life-saving” option for tumors that

were previously considered to be incurable. We anticipate that the next years will be as interesting in terms of the translation of the PD-1/PD-L1 pathway to thyroid precision oncology.

Conclusion

The study found a statistically significant association between PD-L1–positive expression, T stage, size >4 cm, and LN metastasis. PD-L1 expression showed potential to be used as a prognostic marker for patients with PTC. Therefore, PD-1/PD-L1 pathway blockade may be a therapeutic option for patients with advanced thyroid cancer. Further multicenters studies with a larger sample size and comprehensive follow-up are essential to confirm the prognostic and predictive value of PD-L1 in patients with PTC.

Authors' Contributions

A.G.M.E.S. conceptualized and designed the study, collected clinical data, coordinated IHC testing, analyzed results, and drafted the manuscript. D.R.D.I., M.M.E.L., and M.M.A.E.E.D. assisted in data interpretation, literature review, and critical manuscript revision. H.H.A.G. performed histopathological evaluation of PTC specimens, assessed PD-L1 expression through IHC, contributed to the interpretation of pathological findings, and critically revised the manuscript. R.M.F. supervised the entire study, guided the research methodology, provided final approval of the manuscript, and is accountable for all aspects of the work.

Patients' Consent

Written informed consent was obtained from all patients prior to study inclusion.

Funding

None.

Conflict of Interest

None declared.

References

1 Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, cancer incidence and mortality worldwide. IARC CancerBase No. 11. 2013
2 Ferlay J, Colombet M, Soerjomataram I, et al. Cancer statistics for the year 2020: an overview. Int J Cancer 2021;149(04): 778–789
3 Miranda-Filho A, Lortet-Tieulent J, Bray F, et al. Thyroid cancer incidence trends by histology in 25 countries: a population-based study. Lancet Diabetes Endocrinol 2021;9(04):225–234
4 Girolami I, Pantanowitz L, Mete O, et al. Programmed death-ligand 1 (PD-L1) is a potential biomarker of disease-free survival in papillary thyroid carcinoma: a systematic review and meta-analysis of PD-L1 immunoexpression in follicular epithelial derived thyroid carcinoma. Endocr Pathol 2020;31(03):291–300
5 Wang Z, Wu X. Study and analysis of antitumor resistance mechanism of PD1/PD-L1 immune checkpoint blocker. Cancer Med 2020;9(21):8086–8121
6 Chowdhury S, Veyhl J, Jessa F, et al. Programmed death-ligand 1 overexpression is a prognostic marker for aggressive papillary thyroid cancer and its variants. Oncotarget 2016;7(22): 32318–32328
7 Angell TE, Lechner MG, Jang JK, Correa AJ, LoPresti JS, Epstein AL. BRAF V600E in papillary thyroid carcinoma is associated with increased programmed death ligand 1 expression and suppressive immune cell infiltration. Thyroid 2014;24(09):1385–1393
8 Ahn S, Kim TH, Kim SW, et al. Comprehensive screening for PD-L1 expression in thyroid cancer. Endocr Relat Cancer 2017;24(02): 97–106
9 Tuttle RM, Haugen B, Perrier ND. Updated American Joint Committee on cancer/tumor-node-metastasis staging system for differentiated and anaplastic thyroid cancer: what changed and why? Thyroid 2017;27(06):751–756
10 Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin 2017;67(01):7–30
11 An HJ, Ko GH, Lee JH, et al. Programmed death-ligand 1 expression and its correlation with lymph node metastasis in papillary thyroid carcinoma. J Pathol Transl Med 2018;52(01):9–13
12 Bai Y, Niu D, Huang X, et al. PD-L1 and PD-1 expression are correlated with distinctive clinicopathological features in papillary thyroid carcinoma. Diagn Pathol 2017;12(01):72
13 Aghajani MJ, Yang T, McCafferty CE, Graham S, Wu X, Niles N. Predictive relevance of programmed cell death protein 1 and tumor-infiltrating lymphocyte expression in papillary thyroid cancer. Surgery 2018;163(01):130–136
14 Aghajani MJ, Roberts TL, Yang T, et al. Elevated levels of soluble PD-L1 are associated with reduced recurrence in papillary thyroid cancer. Endocr Connect 2019;8(07):1040–1051
15 Mehnert JM, Varga A, Brose MS, et al. Safety and antitumor activity of the anti-PD-1 antibody pembrolizumab in patients with advanced, PD-L1-positive papillary or follicular thyroid cancer. BMC Cancer 2019;19(01):196
16 Marabelle A, Fakih M, Lopez J, et al. Association of tumour mutational burden with outcomes in patients with advanced solid tumours treated with pembrolizumab: prospective biomarker analysis of the multicohort, open-label, phase 2 KEYNOTE-158 study. Lancet Oncol 2020;21(10):1353–1365
17 Lubin D, Baraban E, Lisby A, Jalali-Farahani S, Zhang P, Livolsi V. Papillary thyroid carcinoma emerging from Hashimoto thyroiditis demonstrates increased PD-L1 expression, which persists with metastasis. Endocr Pathol 2018;29(04):317–323
18 Fadia M, Fookeerah P, Ali S, Shadbolt B, Greenaway T, Perampalam S. PD-L1 expression in papillary thyroid cancer with and without lymphocytic thyroiditis: a cross sectional study. Pathology 2020; 52(03):318–322
19 Harahap AS, Lay FK, Kodariah R, Wongkar FJ, Ham MF. Association of programmed death-ligand 1 expression with aggressive histological types of thyroid carcinoma. Cancer Manag Res 2022; 14:3539–3550
20 Wan B, Deng P, Dai W, et al. Association between programmed cell death ligand 1 expression and thyroid cancer: a meta-analysis. Medicine (Baltimore) 2021;100(14):e25315
21 Zantut-Wittmann DE, Barreto IS, Laus AC, et al. PD-L1 and MCL-1 markers and the relationship with prognostic characteristics of differentiated thyroid carcinoma. Mol Cell Endocrinol 2023; 570:111931
22 Neamah AS, Janabi AA. Immunohistochemical expression of PDL1 in papillary thyroid carcinoma and its correlation with clinicopathological parameters. HIV Nurs 2023;23(01):281–284

