Med. J. Cairo Univ., Vol. 90, No. 1, March: 31-38, 2022
www.medicaljournalofcairouniversity.net

Expression of CD10 and CD56 in Benign and Malignant Thyroid Lesions

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Abstract

Background: CD 10 was initially recognised as a cell–surface antigen expressed by acute lymphoblastic leukaemias, and hence it's early designation as Common Acute Lymphoblastic Leukemia Antigen (CALLA). Also, it has been proven to be reactive in various non-lymphoid cells and tissue and different types of neoplasms.

CD56 or neural cell adhesion molecule (NCAM) is a homophilic membrane glycoprotein. It is an adhesion molecule from the immunoglobulin (Ig) superfamily that is expressed normally on the surface of neurons, glia, skeletal muscle cells, and natural killer cells.

Aim of Study: The aim of this work is to study the immunohistochemical expression of CD 10 and CD56 in malignant thyroid neoplasms and different benign lesions and assess whether CD 10 can be used as a malignancy marker in thyroid pathology and whether CD56 can be used to differentiate between follicular variant of papillary thyroid carcinoma (FVPTC) and other follicular-patterned neoplasms [follicular adenoma (FA) and follicular carcinoma (FC)].

Material and Methods: A total of 50 archived, formalin fixed, paraffin embedded tissue blocks of 50 cases of malignant thyroid neoplasms and different benign lesions. The samples were immunohistochemically analysed for CD10&CD56 expressions. A p-value of less than 0.05 was considered statistically significant.

Results: Concerning CD10 immunoreactivity was statistically significant in the malignant lesions (91.2%) compared to benign lesions (56%) (p-value=0.004). CD10 expression was statically significant in higher tumor stages (p=0.048) and in malignant cases with positive LN metastasis (p=0.012).

Concerning CD56 immunoreactivity was statistically significant in the benign lesions (93.8%) compared to malignant lesions (32.4%) (p-value=0.000). There was a statistically significant difference in CD56 immunoreactivity among follicular-patterned lesions (FA, FC and FVPTC) (p-value =0.000). CD56 expression was also statically significant in malignant cases with positive LN metastasis compared to cases not associated with LN metastasis (p-value=0.024).

Conclusion: The results of the current study indicate that CD 10 might be used for differentiating benign and malignant lesions and CD56 can be used to differentiate between follicular variant of papillary thyroid carcinoma and other follicular-patterned neoplasms (follicular adenoma and follicular carcinoma.

Key Words: *Malignant thyroid neoplasms – Benign thyroid lesions – CD10 – CD56.*

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Introduction

THYROID nodules are common in adults, with a reported prevalence of up to 50% **[1]**. Furthermore, 9% to 15% of nodules identified during clinical examinations are diagnosed as malignant **[2]**. Most thyroid lumps are benign, but 5% are malignant and it is important to distinguish this sinister minority. Benign thyroid lumps may include thyroid adenoma, thyroiditis, thyroid cysts and hyperplastic nodules **[3]**. Thyroid cancer is considered as the most common endocrine malignancy. It includes papillary thyroid carcinoma (PTC) (80%), follicular carcinoma (15%), poorly differentiated carcinoma (<1%) and anaplastic thyroid carcinoma (ATC) (<2%) **[4]**.

Thyroid carcinoma constitutes for 1 % of all cancers. Its incidence has significant geographic variation **[5]**. It is estimated that the incidence rate of thyroid carcinoma ranging from 0.5-10 cases per 100, 000 world-wide **[6]**. In Egypt, according to the National Cancer Registry Program, thyroid cancer is the fifth most frequent cancer in females accounting for 3.6% of all malignancy in women. The incidence ranged between 3.5% in Upper Egypt in 2008 to 3.9% in 2011 in Lower Egypt. The estimated number of thyroid cancer in Egypt in 2015 was 2448 cases of whom 1876 were females **[7]**.

The most common histopathological type of thyroid carcinoma is papillary thyroid carcinoma (PTC) which accounts to a percentage of 80% of all thyroid carcinomas in adults **[8,9]**. The diagnosis

of PTC depends upon the structural characteristics together with nuclear clearing, overlapping, intranuclear grooves and intra-nuclear pseudo inclusions. The diagnosis of PTC based on these standards is still the most effective method in the classical unequivocal cases [10]. However, some of these morphological features can be found in other benign and malignant thyroid lesions, which can represent diagnostic challenge [11]. To overcome this problem different cytological, immunohistochemical and molecular studies have been developed [12].

CD 10 was initially identified as a cell–surface antigen expressed by acute lymphoblastic leukemias, and hence its early designation as Common Acute Lymphoblastic Leukemia Antigen (CALLA). This antigen is widely used for the categorization of acute leukemias and for the subclassification of malignant lymphomas [13]. CD10 is a single-chain, 90-110-KDa cell surface zinc dependent metalloprotease that inactivates various bioactive neuropeptides [14]. In addition to its enzymatic function, the CD 10 protein has a direct role in signal transduction pathways that regulate cell growth and apoptosis and because of its structural similarity to the matrix metalloproteases in the stroma, CD10 is thought to affect invasion and metastatic potential of tumor cells by altering the cellular microenvironment [15].

Oh et al., 2020 concluded that the expression of CD 10 might be implicated in the early stage of PTC development, but CD10 expression had no impact on prognosis in PTC patients [16].

FVPTC is the most common variant and is also the one that has generated a lot of controversy in its diagnosis [17]. FVPTC manifests overlapping histopathological features with other follicular-patterned thyroid neoplasms (FA and FC), and thus, not infrequently, poses a diagnostic challenge for pathologists [18].

Many immunohistochemical markers were suggested for the differential diagnosis of these lesions. CD56 is a neural cell adhesion molecule, a transmembrane protein that is expressed in activated T lymphocytes, NK cells, neural and endocrine tissue. Its expression could regulate the cellular motility and migratory capacity, as well as reduce the invasion and metastasis of tumor [19]. Pyo et al., 2018 concluded that the rate of loss of CD56 immunohistochemistry expression was significantly higher in malignant tumors, such as PTC and FC, than in FA, nodular thyroid hyperplasia (NH), and Hashimoto's thyroiditis [19].

Material and Methods

The material of this study consists of fifty cases of both benign and malignant thyroid lesions (16 and 34 respectively). All specimens were collected from the Pathology Department, Faculty of Medicine, Al-Azhar University. The period of case collection was from June 2019 up to September 2020. The clinical data of these patients including age and sex were taken from their pathology requisition sheets enclosed with the specimens.

Processing:

Sections of 4-µm thickness were cut by microtome from the formalin fixed, paraffin embedded tumor blocks. Three sections were prepared from each tumor tissue paraffin block:

- One slide for Hematoxylin and Eosin (H&E) staining for histopathological reassessment.
- Two positively charged slides for immunohistochemical staining by CD 10 & CD56 monoclonal antibodies.
- All slides were examined under light microscope.

Immunohistochemical methods:

Serial paraffin sections from all cases were stained immunohistochemically for CD10 & CD56 monoclonal antibodies using a standard indirect immunoperoxidase antiperoxidase (PAP) technique (detailed below).

A- *Monoclonal antibodies used:*

I- CD10 (Clone GM003) is a mouse monoclonal antibody. It is designed for the specific localization of CD 10 receptors in formalin fixed, paraffin embedded tissue (Genemed, South San Francisco, CA, USA, dilution 1:50).

II- CD56/NCAM (clone 123C3) is a purified mouse monoclonal IgG1 antibody (Genemed Biotechnologies, Inc CA94080, USA). It was received as 6ml prediluted ready to use.

B- *Methodology for CD10:*

Steps:

1- After routine deparaffinization in xylene, the sections were hydrated through a series of graded alcohols (100%-95%-70%) 5 minutes each, distilled water for 5 minutes, and phosphate buffered saline (PBS) for 5 minutes.

2- For antigen retrieval, the slides were treated by microwave heating in citrate buffer (pH 9.0) for 15 minutes.

3- 3% hydrogen peroxide (H_2O_2) was used for blocking endogenous peroxidase activity.

4- The sections were then incubated with monoclonal mouse CD 10 antibody clone GM003 (Genemed, South San Francisco, CA, USA) at 1:50 dilution for one hour at room temperature.

5- After washing in phosphate buffered saline, the samples were incubated with a biotin conjugated secondary antibody and then incubated using streptavidin-biotin system for 30 minutes at room temperature.

6- The reactions became visible after immersion of the specimens in 3,3-diaminobenzidine tetra hydrochloride (DAB).

7- The sections were counterstained with Mayer's Hematoxylin stain, then rinsed and mounted.

C- *Methodology for CD56:*

The same procedures mentioned above for CD 10, but with using monoclonal antibody of CD56.

Interpretation of immunostaining:

A- CD10 interpretation:

In the present study sections obtained from tonsils were used as positive control of CD10, which exhibited strong intensity of CD 10 immunostaining.

Negative control was performed by omitting CD 10 antibody during the primary antibody incubation.

Brown cytoplasmic with or without membranous staining is defined as CD 10 positivity.

For each case, 10 high power fields were evaluated. Mean percentage of positive cells <10% and 10% are considered as negative and positive respectively. The immunoreactivity interpreted based on the percentage of the stained cells irrespective of the intensity of the staining **[20]**.

B- CD56 interpretation:

Normal thyroid tissue was used as positive control of CD56, which exhibited strong intensity of CD56 immunostaining.

Negative control was performed by omitting CD56 antibody during the primary antibody incubation.

Brown membranous staining either associated or not with cytoplasmic expression defined as CD56 positivity.

For each case, membranous staining in more than 10% of cells was required to assign its positivity either associated or not with cytoplasmic expression **[21]**.

Statistical methods:

All analyses were done using SPSS (Statistical Package for Social Sciences) software, version 21, Chicago, IL, USA. Categorical variables were expressed as frequencies and percentages. Chi-square test was used for testing proportion independence to rule out any significant correlation between CD10 & CD56 expression and other clinicopathological variables included in the study. *p*-value was set significant if 0.05 level.

Results

Clinicopathological characteristics of the studied cases and their correlation with CD 10 expression are summarised in (Table 1).

Table (1): Clinicopathological characteristics of the studied cases and their correlation with CD 10 expression.

Parameter	Number (%)	CD 10 (Negative) expression	CD 10 (Positive) expression	*p*-value
Age:				
<55 yeas	37 (74%)	8 (21.6%)	29 (78.4%)	0.417
55 years	13 (26%)	2 (15.4%)	11 (84.6%)	
Gender:				
Male	10 (20%)	2 (20%)	8 (80%)	1.000
Female	40 (80%)	8 (20%)	32 (80%)	
Category:				
Malignant	34 (68%)	3 (8.8%)	31 (91.2%)	0.004
Benign	16 (32%)	7 (43.7%)	9 (56.3%)	
Pathological tumor stage:				
T1	10 (29.4%)	3 (30%)	7 (70%)	0.048
T2	12 (35.3%)	0 (0%)	12 (100%)	
T3	8 (23.5%)	0 (0%)	8 (100%)	
T4	4 (11.8%)	0 (0%)	4 (100%)	
Lymph node metastasis:				
NX	21 (61.76%)	0 (0%)	21 (100%)	0.012
N0	5 (14.71%)	3 (60%)	2 (40%)	
N1	8 (23.53%)	0 (0.0%)	8 (100%)	
Histological types:				
PTC	23 (46%)	2 (91.3%)	21 (8.7%)	0.099
FC	7 (14%)	1 (14.3%)	6 (85.7%)	
ATC	2 (4%)	0 (0%)	2 (100%)	
MTC*	2 (4%)	0 (0%)	2 (100%)	
NH	6 (12%)	2 (33.3%)	4 (66.7%)	
FA	10 (20%)	5 (50%)	5 (50%)	
Follicualr-patterned lession:				
FVPTC	2 (20%)	8 (80%)	10 (37.03%)	0.129
FC	1 (14.3%)	6 (85.7%)	7 (25.94%)	
FA	5 (50%)	5 (50%)	10 (37.03%)	

*MTC = Medullary thyroid carcinoma.

CD10 protein expression:

CD 10 immunostaining was identified in (40/50) (80%) of the studied cases, while only (10/50) (20%) of the studied cases showed negative CD 10 expression.

Studied cases are categorized into two groups (benign and malignant). Whereas (31/34) (91.2%) of malignant cases showed positive CD 10 expression, only (3/34) (8.8%) showed negative CD 10 expression. Regarding benign cases while (9/16) (56.3%) of benign cases showed positive CD10 expression, the remaining (7/16) (43.8%) showed negative CD10 expression. The difference in expression between benign and malignant tumours was statistically significant (p-value = 0.004) (Table 1).

CD 10 immunostaining was identified in (21/23) (91.3%) of PTC [(13/13) (100%) of conventional papillary thyroid carcinoma (CPTC) and (8/10) (80%) of FVPTC], (6/7) (85.7%) of FC, (5/10) (50%) of FA and (4/6) (66.7%) of NH, (2/2) (100%) of ATC & (2/2) (100%) of MTC (Table 1). The difference in expression among different histological types was statistically insignificant (p-value =0.099) (Table 1) (Fig. 1).

CD 10 expression was detected in (8/10) (80%) of males and (32/40) (80%) of females, so there was no difference in CD10 expression between males and females indicating a statistically insignificant correlation (p-value=1.000).

Correlation between CD 10 expression and age among studied cases was statistically not significant (p-value=0.417).

Correlation between CD 10 expression and pathological tumor stage (pT) among studied malignant cases was statistically significant (p-value=0.048), where higher stages showed CD 10 positive expression. As shown in the previous table (24/24) (100%) of (T2, T3 & T4) cases showed CD10 positive expression, but only (7/10) (70%) of (T1) cases showed CD 10 positive expression.

Correlation between CD 10 expression and LN metastasis among studied malignant cases was statistically significant (p-value=0.012), where all cases with positive LN metastasis (8/8) (100%) showed CD10 positive expression and only (2/5) (40%) of cases with negative LN metastasis showed CD 10 positive expression.

Follicualr-patterned lesions represented (27/50) (54%) of the studied cases. CD 10 expression was detected in (6/7) (85.7%) of FC, (5/10) (50%) of FA and (8/10) (80%) of FVPTC. The difference in expression among follicular-patterned lesions was statistically insignificant (p-value=0.129).

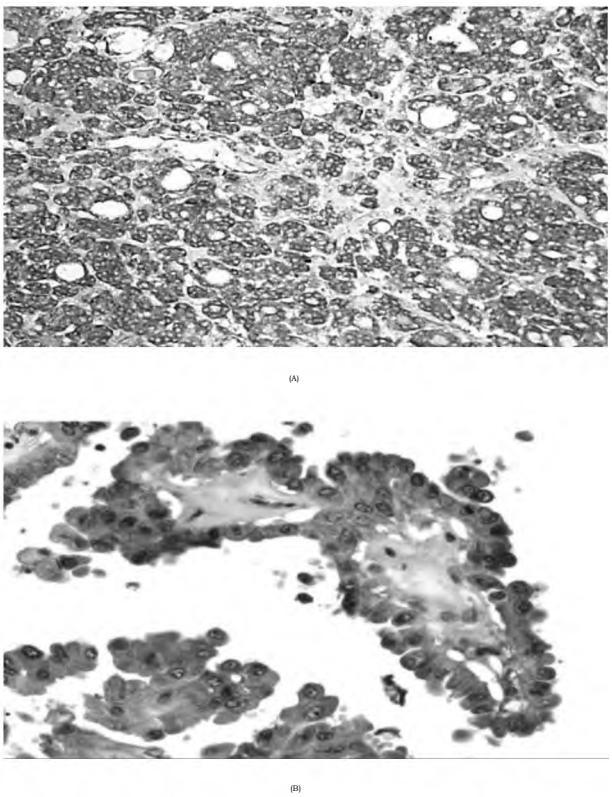

Fig. (1): CD10 expression: (A) Follicular adenoma showing positive CD 10 cytoplasmic and membranous staining (IHC x 100). (B) Papillary thyroid carcinoma showing positive CD 10 cytoplasmic and membranous staining (IHC x 400).

Clinicopathological characteristics of the studied cases and their correlation with CD56 expression are summarised in (Table 2).

CD56 protein expression:

CD56 immunostaining was identified in (26/50) (52%) of the studied cases, while only (24/50) (48%) of the studied cases showed negative CD56 expression.

Regarding malignant cases, whereas (23/34) (67.6%) showed negative CD56 expression, only (11/34) (32.4%) of malignant cases showed positive CD56 expression. Regarding benign cases while (15/16) (93.8%) of benign cases showed positive CD56 expression, only (1/16) (6.3%) showed negative CD56 expression. The difference in expression between benign and malignant tumours was statistically significant (p-value=0.000).

CD56 immunostaining was identified in (2/23) (8.7%) of PTC [(2/13) (15.4%) of CPTC and (0/10)

(0%) of FVPTC], (6/7) (85.7%) of FC, (9/10) (90%) FA, (6/6) (100%) of NH, (1/2) (50%) of ATC and (2/2) (100%) of MTC (Table 2). The difference in expression among different histological types was statistically significant (p-value =0.000) (Table 2) (Fig. 2).

Table (2): Clinicopathological characteristics of the studied cases and their correlation with CD56 expression.

Parameter	Number (%)	CD56 (Negative) expression	CD56 (Positive) expression	p-value
Age:				
<55 yeas	37 (58%)	22 (59.5%)	15 (40.5%)	0.000
55 years	13 (42%)	2 (15.4%)	11 (84.6%)	
Gender:				
Male	10 (20%)	5 (50%)	5 (50%)	0.887
Female	40 (80%)	19 (47.5%)	21 (52.5%)	
Category:				
Malignant	34 (68.7%)	23 (67.6%)	11 (32.4%)	0.000
Benign	16 (31.3%)	1 (6.3%)	15 (93.8%)	
Pathological tumor stage:				
T1	10 (29.4%)	10 (100%)	0 (0%)	0.026
T2	12 (35.3%)	8 (66.7%)	4 (33.3%)	
T3	8 (23.5%)	4 (50%)	4 (50%)	
T4	4 (11.8%)	1 (25%)	3 (75%)	
Lymph node metastasis:				
NX	21 (61.76%)	15 (71.4%)	6 (28.6%)	0.024
N0	5 (14.71%)	5 (100%)	0 (0%)	
N1	8 (23.53%)	3 (37.5%)	5 (62.5%)	
Histological types:				
PTC	23 (46%)	21 (91.3%)	2 (8.7%)	0.000
FC	7 (14%)	1 (14.3%)	6 (85.7%)	
ATC	2 (4%)	1 (50%)	1 (50%)	
MTC	2 (4%)	0 (0%)	2 (100%)	
NH	6 (12%)	0 (0%)	6 (100%)	
FA	10 (20%)	1 (10%)	9 (90%)	
Follicualr-patterned lession:				
FVPTC	10 (37.03%)	10 (100%)	0 (0%)	0.000
FC	7 (25.94%)	1 (14.3%)	6 (85.7%)	
FA	10 (37.03%)	1 (10%)	9 (90%)	

CD56 expression was detected in (5/10) (50%) of males and (21/40) (52.5%) of females, so the difference in expression between males and females was statistically insignificant (p-value=0.887).

Correlation between CD56 expression and age among studied cases was statistically significant (p-value=0.000), where the mean age of cases with positive CD56 expression (50.38 Y) was older than that of cases with negative CD56 expression (36 Y).

Correlation between CD56 expression and pathological tumor stage (pT) among studied malignant cases was statistically significant (p-value=0.026), where positivty was seen more in higher stages cases, so that (3/4) (75%) and (4/8) (50%) of T4 and T3 cases respectively showed CD56 positive expression, while only (4/12) (33.3) of T2 cases showed CD56 positive expression and none (0/10) (0%) of T1 cases showed CD56 positive expression.

Correlation between CD56 expression and LN metastasis among studied malignant cases was statistically significant (p-value=0.024), where (5/8) (62.5%) of cases with positive LN metastasis showed CD56 positive expression and none (0/5) (0%) of cases with negative LN metastasis showed CD56 positive expression.

While CD56 expression was detected in (6/7) (85.7%) of FC, (9/10) (90%) of FA, it was not expressed in all cases of FVPTC (0/10) (0%). The difference in expression among follicular-patterned lesions was statistically significant (p-value=0.000).

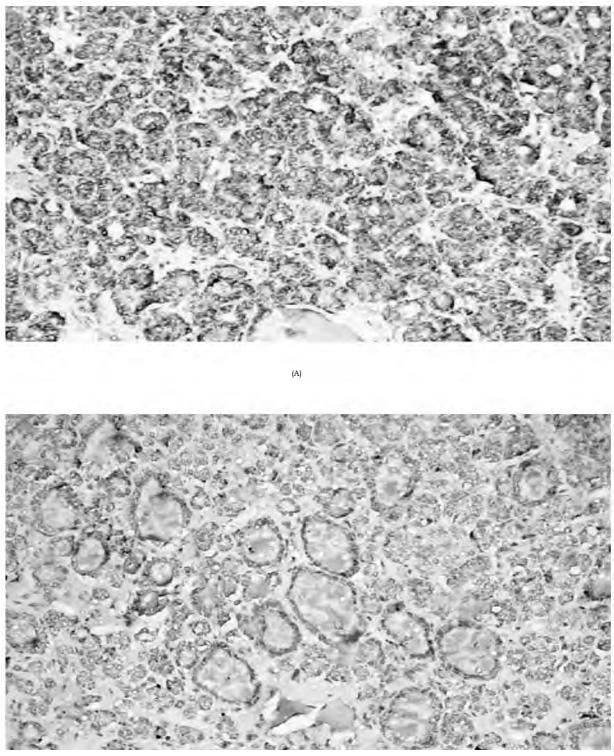

Fig. (2): CD56 expression: (A) Follicular thyroid adenoma showing positive CD56 membranous staining (IHC x 100). (B) Nodular thyroid hyperpalsia showing positive CD56 membranous staining (IHC x 100).

Discussion

In the current study there was a significant correlation between CD 10 expression in benign and malignant lesions (p-value =0.004). Similarly Nakazawa et al., 2018 reported that while most of malignant cases (77/127) (60.6%) showed positive CD10 expression, only (4/25) (16%) of benign cases showed positive CD 10 expression (p-value <0.005) [22].

On the contrary, Yegen et al., 2009 reported an insignificant correlation between CD 10 expression in benign and malignant lesions (p-value >0.05) [23]. This might be due to using antibodies of different nature.

In this study there was an insignificant correlation between CD10 expression and different histological types of studied cases (p-value=0.099). These results were not in agreement with Gabal et al., 2018 who reported a significant correlation between CD 10 expression and different histological types of studied cases (p-value=0.030) [24]. Differences may be due to different scoring systems or may be due to using antibodies of different nature.

In the present study, there was a significant correlation between CD 10 expression and pathologic tumor stage among malignant cases (p-value =0.048). Similar results were reported by Heshmati et al., 2017 (p-value <0.05) [25].

This was in disconcordance to results reported by Oh et al., 2020 who reported an insignificant correlation between CD 10 expression and pathological T stage of the tumors among malignant cases (p-value=0.164) [16]. Such difference may be due to using antibodies of different nature.

In this study, there was a significant correlation between CD 10 expression and LN metastasis among studied malignant cases (p-value=0.012). These results were in disagreement with Oh et al 2020 who found an insignificant correlation between CD10 expression and LN metastasis (p-value=0.143) [16]. Such difference may be due to different scoring system used or may be due to using antibodies of different nature.

In the current study, there was an insignificant correlation between CD 10 expression in follicular-patterned lesions (p-value=0.160). This was not in agreement with Tomoda et al., 2003 who reported a significant correlation between CD 10 expression in follicular-patterned lesions (p-value <0.05) [26]. Such difference may be due to using different antibodies of different nature.

Regarding CD56, in the current study, there was a significant correlation between CD56 expression in in benign and malignant lesions (p-value=0.000). Similar results were reported by Shameem et al., 2020 (p-value=0.0001) [28].

In the present study the correlation between CD56 expression and different histological types of studied cases was statistically significant (p-value=0.000). Similar results were reported by Tastekin et al., 2019 and Muthusamy et al., 2018 (p-value <0.01) [27,29]. Differences in the percentages may be due to the differences in the number of studied cases.

Correlation between CD56 expression and pathological tumor stage (pT) among studied malignant cases was statistically significant (p-value=0.026). On the contrary, Muthusamy et al., 2018 reported an insignificant correlation between CD56 expression and pathological T stage of the studied malignant cases (p-value=0.126) [29]. This might be explained by different scoring systems or may be due to using antibodies of different nature.

In the current study, there was a significant correlation between CD56 expression and LN metastasis among malignant lesions (p-value =0.024). On the contrary, Muthusamy et al., 2018 reported an insignificant correlation between CD56 expression and LN metastasis (p-value=0.076) [29]. The difference may be due to using antibodies of different nature.

In this study, there was a significant correlation between CD56 expression in follicular-patterned lesions (p-value=0.000). Similar results were reported by Golu et al., 2017 (p-value=0.008) [30]. Differences in the percentages may be due to the differences in the number of studied cases.

In conclusion, CD 10 expression is a statistically significant in malignant lesions compared to benign lesions. Conversely, CD56 expression is a statistically significant in benign lesions compared to malignant lesions. Accordingly, using a panel of CD10 and CD56 will give more accurate results in diagnoses of both benign and malignant lesions.

CD10 is of no value in differentiating the FVPTC from either FA or FC. However, CD56 expression is a statistically significant in FA and FC compared to FVPTC, so CD56 will be valuable in differentiating FVPTC from either FA or FC. This is especially useful when making decision in thyroid lesions showing equivocal in conclusive nuclear features.

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التعبير المناعى الهستوكيميائى لكل من سى دى ١٠ وسى دى ٥٦ فى أورام الغدة الدرقية الحميدة والخبيثة

\المقدمة: سرطان الغدة الدرقية هو من أكثر السرطانات شيوعاً، حيث يمثل ١٪ من سرطانات البالغين و ٣٪ من سرطانات الأطفال، وهو يمثل خامس أكثر السرطانات انتشاراً بين الأناث ، وهناك تحديات وصعوبات فى تشخيص بعض فصائل هذا السرطان ، ولذا تجرى العديد من الأبحاث للتوصل إلى طرق تسهل التشخيص الدقيق لهذه الفصائل، واحدى هذه الطرق هى الكواشف المناعية.

\الأهداف: دراسة التعبير المناعى الهستوكيميائى لكل من (سى دى ١٠) و (سى دى ٥٦) فى أورام الغدة الدرقية الحميدة والخبيثة ، وتقييم دور الـ (سى دى ١٠) فى تشخيص الأورام الخبيثة للغدة الدرقية، وتقييم دور الـ (سى دى ٥٦) فى تمييز الفصيل الجريبى للسرطان الحليمى عن با قى الأورام الجريبية.

\الطرق: الدراسة على ٥٠ عينة من أورام الغدة الدرقية (الحميدة والخبيثة)، تم جمعها من قسم الباثولوجى، كلية الطب، جامعة الأزهر خلال الفترة من يونيو ٢٠١٩ حتى سبتمبر ٢٠٢٠.

\النتائج: فيما يتعلق بالكاشف المناعى (سى دى ١٠) تم التعبير عنه فى ٤٠ حالة (٨٠٪) من الحالات المدروسة، وتم تأكيد ارتباط التعبير المناعى له بحالات الأورام الخبيثة (p=0.004)، فيما يتعلق بالكاشف المناعى (سى دى ٥٦) تم التعبير عنه فى ٢٦ حالة (٥٢٪) من الحالات المدروسة، وتم تأكيد دوره فى تمييز الفصيل الجريبى للسرطان الحليمى عن با قى الأورام الجريبية (p=0.000).

\الخلاصة: خلصنا إلى أن (سى دى ١٠) ربما يستخدم ككاشف مناعى لتشخيص الأورام الخبيثة للغدة الدرقية، وأن (سى دى ٥٦) ربما يستعمل ككاشف مناعى لتمييز الفصيل الجريبى للسرطان الحليمى عن باقى الأورام الجريبية الحميدة والخبيثة.