e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(12); 700-708

Original Research Article

The Expression of CD56 to Distinguish Papillary Carcinoma of Thyroid (Including its Variants) from Other Thyroid Lesions

Hemaxi R Patel[1], Paras G Patel[2], Ankita A Shah[3], Jignesh D Patel[4]

[1]Tutor Pathology Department, GMERS Medical College, Panchmahal Godhra, Gujarat.

[2]Associate Professor Pathology Department Surat Municipal Institute of Medical Education &Research, Surat, Gujarat

[3]Head of IHBT Department, Surat Municipal Institute of Medical Education &Research, Surat, Gujarat

[4]Third Year Resident, DM Cardiology, UN Mehta Institute of Cardiology and Research Centre, Ahmedabad, Gujarat

Received: 25-11-2022 / Revised: 15-12-2022 / Accepted: 23-12-2022
Corresponding author: Dr Jignesh D Patel
Conflict of interest: Nil

Abstract

Aim of study: The main aim is to study the applicability of difference in CD56 expression as a marker that distinguishes papillary carcinoma of thyroid (including its variants) from other thyroid lesion.

Methods: The study was conducted in department of the Pathology, SMIMER medical college, Surat. Surgically removed and formalin-fixed thyroid specimens were collected and processed for histopathological examination by H& E stain and immunohistochemical examination by CD56 IHC marker. Thyroid lesion were surgically removed and formalin – fixed specimen were received. After grossing specimen was kept for 24 hours with10% formalin for proper fixation, subsequently, dehydration by graded alcohol, clearing by xylene and embedding in paraffin wax was carried out. Blocks were made and serial sections of 3-5 micron thickness were taken and stained with haematoxylin and eosin (H & E). All 55 cases were subjected to Immunohistochemical staining with Monoclonal Mouse Antihuman CD56 antibody of Dako Company, clone 123C3, Lot 20049679 and ready to use.

Only single variable staining density in neoplastic cells recorded. IHC staining was interpreted with an optical microscope under 10x and 40x magnification. For positive control, normal thyroid gland in the same specimen was considered. The strong and complete membranous expression with or without cytoplasmic staining of the tumor cells qualified the case as positive for CD56.

Results: The present study was conducted on a total of 55 lesions. In present study there were 3 cases of papillary thyroid carcinoma out of which two cases were conventional papillary thyroid carcinoma and one case was follicular variant of papillary thyroid carcinoma. All three cases of papillary thyroid carcinoma were negative for CD56.There were 3 cases of well differentiated tumor of unknown malignant potential and all three were negative for CD 56.

Conclusion: In this study CD56 expression was absent in Papillary carcinoma and that CD56 expression retained in majority of benign thyroid lesions.CD56 expression allowed the differentiation of papillary thyroid carcinoma from non-neoplastic lesions and other thyroid tumor derived from follicular cells with very high sensitivity and specificity.

Keywords: CD56, Thyroid papillary carcinoma, Histopathological examination, Immunohistochemistry

Introduction

Thyroid Cancer Represents About 5 -24 % Of Thyroid Nodules And 1-2% Of All Malignancies. [1] Papillary Thyroid Carcinoma Is The Most Common Type Of Thyroid Carcinoma And The Most Common Endocrine Malignancy [1].It Is More Commonly Seen In Females. It Can Occur At Every Age, But Is More Common In Young And Middle-Aged Adults; The Median Age At Diagnosis Is 40 Years. [2] It Is Caused By Environmental, Genetic And Hormonal Factors. In Children Especially, The Etiology Is Associated With Radiation To The Neck Area.

Macroscopically Most Cases Are Solid, Whitish, Firm And Invasive; 10% To 20% Are Surrounded By A Complete Capsule [3]. Microscopically, The Typical Papillary Carcinoma Contains Numerous True Papillae [4]. Papillae Are Usually Complex, Branching, And Randomly Oriented, With A Central Fibro Vascular Core And A Single Or Stratified Lining Of Cuboidal Cells [5].Cells Having Ground Glass Nuclei, Invagination Of Cytoplasm Appear As Round Acidophilic Vacuoles And Inconspicuous Nucleoli [6,7].Nucleus Contain Groove Arranged Along Longest Nuclear Axis [8]. Nuclear Clearing Is Due To Accumulation Of Fine Threadlike Fibrils [9].

Mitosis Is Usually Very Scanty Or Absent In Papillary Carcinoma [10].Over Half Of The Cases Show Extensive Fibrosis Present From Sclerohyaline To Highly Cellular With Elastic Tissue [11]. Psammoma Body Is A Basophilic Structure Showing Concentric Laminations And Arises From Necrosis Of Individual Tumor Cells [12]. Follicular Variant Of Papillary Carcinoma Composed Entirely Of Follicles [13,14]. It Is Also Referred To As Lindsay Tumour [15, 16].

Papillary Thyroid Carcinoma Has A Large Number Of Morphological Variants. The Most Common Of These Is The Follicular Variant Of PTC (FVPTC), And Its Differentiation From The Other Benign Follicular Patterned Lesions Of The Thyroid Is Usually Very Difficult. The Most Common Follicular Patterned Lesions With Similarities To FVPTC Are Follicular Adenomas, Hyperplastic Nodules And Dysplastic Foci Of Lymphocytic Thyroditis. Severe Chronic Lymphocytic Thyroiditis, Hashimoto's Thyroiditis And Reactive Atypical Attributed To Inflammation Result In Nuclear Morphology Similar To That Of Papillary Carcinoma, With Nuclear Enlargement, Chromatin Clearing And Even Grooves. [17]

There For, The Diagnosis Of Noninvasive, Encapsulated Follicular Variant Of Papillary Thyroid Carcinoma Versus Follicular Adenoma Is Prone To Considerable Inter Observer Variability.

CD56 Is A Hemophilic Membrane Glycoprotein Found In Normal Thyroid Follicular Epithelial Cells. It Is An Adhesion Molecule From The Immunoglobulin Super Family That Is Expressed Normally On The Surface Of Neurons, Glia, Skeletal Muscle Cells And Natural Killer Cells .It Regulates Cell Motility And Affects The Migration Capacity Of Tumor Cells.

CD56 Present On Follicular Epithelial Cells Of The Normal Thyroid Shows Diffusely Membranous Staining. [18]

CD56 Can Help In Differentiating Papillary Thyroid Carcinoma From Benign Thyroid Lesions. [19]

Mokhtari Et Al (2013) --- Studied A Total No. Of 146 Cases. Out Of 146 Cases73 Cases Were Papillary Thyroid Carcinoma And Out Of 73 PTC Cases 72 Cases Were CD56 Negative.CD56 Sensitivity And Specificity In Their Study Was 98.6%% And 95.8 Respectively. They Concluded That CD56 Is Both A Sensitive And Specific Marker For Differentiating PTC From Other Follicular Lesions Of Thyroid. [20]

Muthusamys Et Al (2018) --- Studied A Total No. Of 108 Cases And They Concluded That CD56 Is A Potentially Good Immunohistochemical Marker For Differentiating Papillary Thyroid Carcinoma From Other Benign Follicular Lesions Of The Thyroid Lesions Especially In Differentiating Follicular Variant PTC From FA In Equivocal Cases. [21]

Material and Methods:

Total 55 Thyroid Lesions Were Sent From ENT And Surgery Department To The Pathology Department. Prospective Observational Study Was Done At Pathology Department Of SMIMER, Surat From April 2018 To September 2019.

All Cases Taken Received In 18 Months. Total 55 Cases Was Taken For Study

Inclusion Criteria: Thyroid Lesion Presented As Thyroid Nodule (Both Non Neoplastic And Neoplastic Lesions Are Included.

Exclusion Criteria: Recurrent Thyroid Lesion.

Patients Who Are Not Giving Consent For This Study.

Sample Collection And Procedure: [22]

Thyroid Lesion Were Surgically Removed And Formalin – Fixed Specimen Were Received After Grossing Specimen Was Kept For 24 Hours With10% Formalin For Proper Fixation, Subsequently, Dehydration By Graded Alcohol, Clearing By Xylene And Embedding In Paraffin Wax Was Carried Out.

Blocks Were Made And Serial Sections Of 3-5 Micron Thickness Were Taken And Stained With Haematoxylin And Eosin (H &E).

All 55 Cases Were Subjected To Immuno-histochemical Staining With Monoclonal Mouse Antihuman CD56 Antibody Of Dako Company, Clone 123C3, Lot 20049679 And Ready To Use.

Interpretation: [23]

IHC Staining Was Interpreted With An Optical Microscope Under 10x And 40x Magnification. For Positive Control, Normal Thyroid Gland In The Same Specimen Was Considered. The Strong And Complete Membranous Expression With Or Without Cytoplasmic Staining Of The Tumor Cells Qualified The Case As Positive For CD56.

The Result Was Scored In A Semi Quantitative Manner With Respect To The Percentage Of Positive Tumor Cells [17].

Score% Of Positive Lesional Cells

< 10%Of The Lesional Cells

1+10- 25% Of The Lesional Cells

2+26 -50% Of The Lesional Cells

3+> 50% Of The Lesional Cells

The Percentage Of Positive Cells For Each Section Was Counted Under 5 High Power Fields, And The Mean Value Of Each Was Scored.

1. Score 0 Was Considered Negative.
2. Scores Of 1-3 Were Considered Positive For CD56.

Variable Was Observed By Two Pathologists, Assistant Professor And Associate Professor Of SMIMER PATHOLOGY Department. Both Have

Experience In Histopathology And Immunohistochemistry For More Than 10 Years And No Bias Was Observed.

Data Was Analysed Using SPSS Software Version 20 And Depicted Using Sensitivity, Specificity, Positive Predictive Value And Negative Predictive Value.

Results:

In The Present Study, A Total Of 55 Thyroid Specimens Were Evaluated.

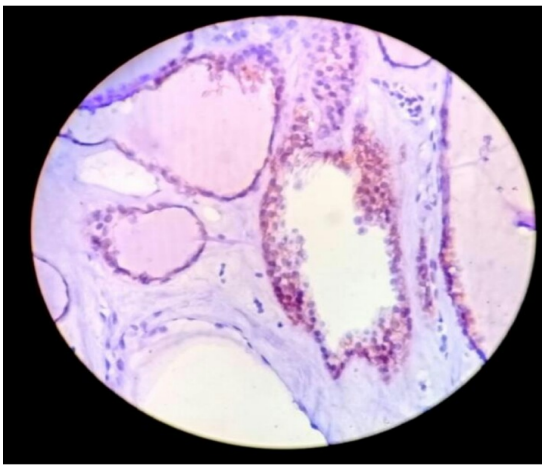

Figure 1: CD 56 IHC in colloid goiter 40x magnification

In figure 1 CD56 shows strong membranous positivity in >50% of lesional cells.

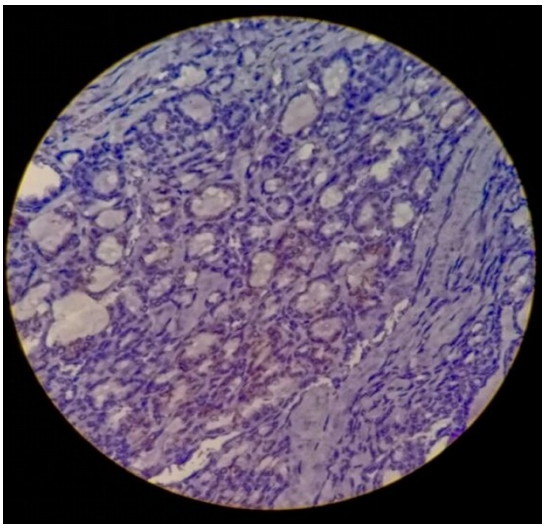

Figure 2: CD 56 IHC in Follicular carcinoma 40 magnification

In figure 2 CD56 Shows strong membranous positivity in10-25% of lesional cells.

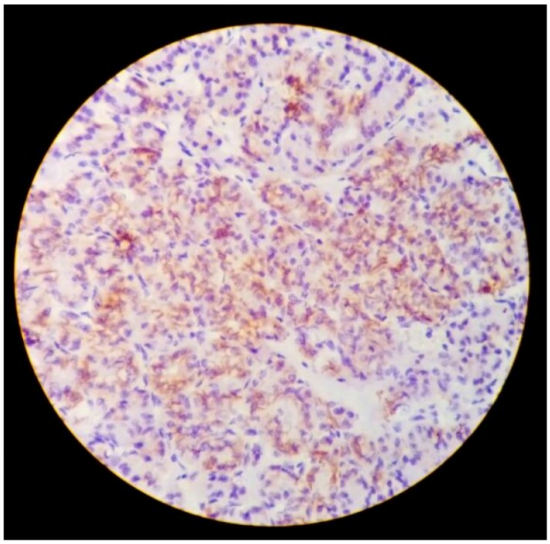

Figure 3: CD 56 IHC in Nodular goiter 40x magnification

In figure 3 CD56 Shows strong membranous positivity in>50% of lesional cells.

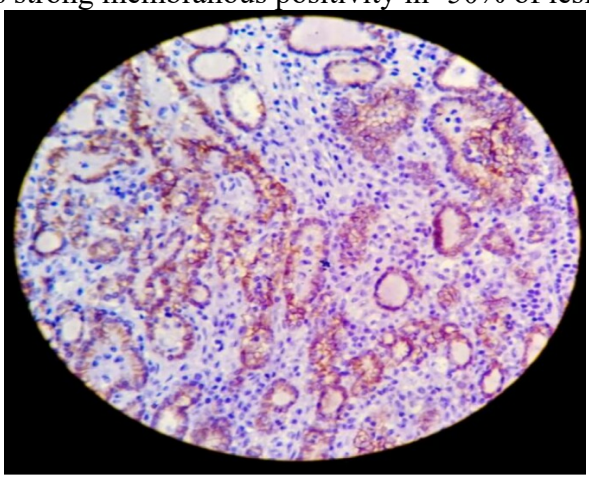

Figure 4: CD 56 IHC in Thyroiditis 40x magnification

In figure 4 CD56 Shows strong membranous positivity in >50% of lesional cells.

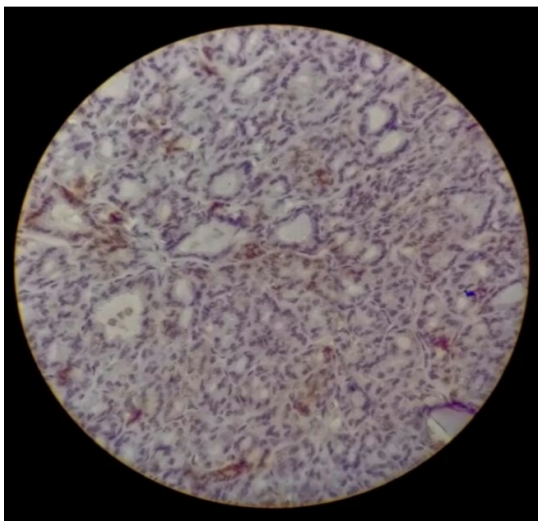

Figure 5: CD 56 IHC in Follicular adenoma 40 magnification

In figure 5 CD56 Shows strong membranous positivity in 26-50% of lesional cells.

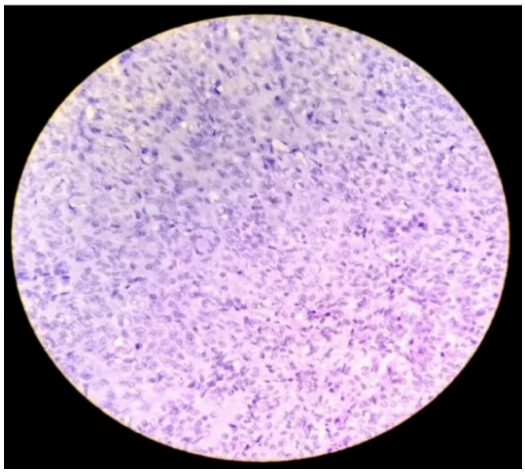

Figure 6: CD 56 IHC in Papillary thyroid carcinoma 40x magnification

In figure 6 CD56 expression was absent.

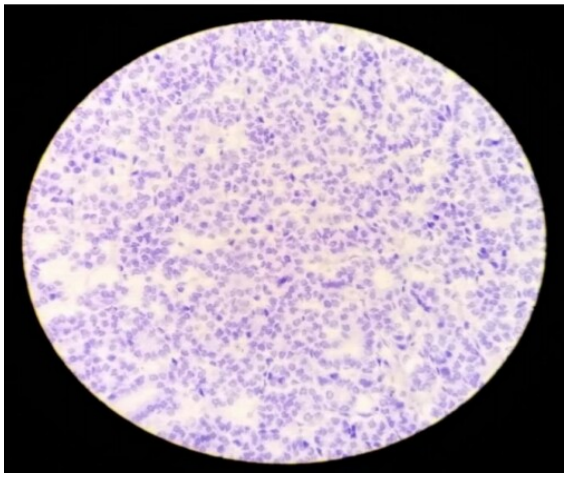

Figure 7: CD 56 IHC in Well differentiated tumors of unknown malignant potential 40x magnification

In figure 7 CD56 expression was absent.

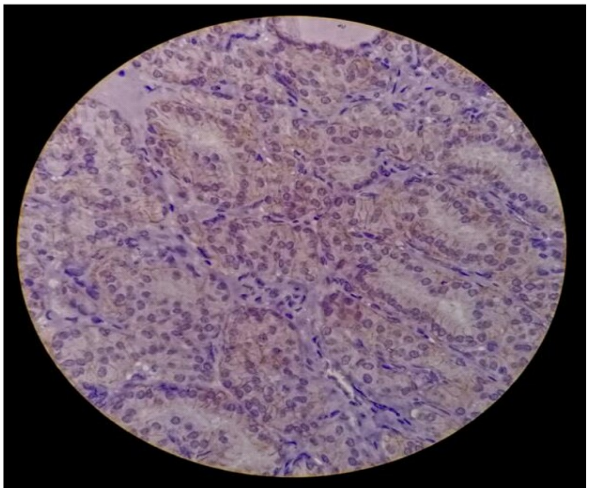

Figure 8: CD 56 IHC in Adenomatoidgoiter40x

In figure 8 CD56 Shows strong membranous positivity in > 50% of lesional cells.

Table 1: Study of CD56 IHC in different thyroid lesions.

Histological diagnosis	No of cases	IHC Result(Score) & percentage			
		0	1	2	3
Colloid goiter	16	0(0)	6(37.5)	3(18.75)	7(43.75)
Nodular goiter	13	0(0)	2(15.38)	2(15.38)	9(69.23)
Adenomatoid goiter	5	2(40)	2(40)	1(20)	0(0)
Cystic Colloid nodule	1	0(0)	1(100)	0(0)	0(0)
Thyroiditis	9	0(0)	3(33.33)	1(11.11)	5(55.56)
Follicular adenoma	4	0(0)	2(50)	2(50)	0(0)
Papillary Thyroid carcinoma	3	3(100)	0(0)	0(0)	0(0)
Follicular carcinoma	1	0(0)	1(100)	0(0)	0(0)
Well differentiated tumor of unknown malignant potential	3	3(100)	0(0)	0(0)	0(0)

In our study Colloid Goiter and Nodular Goiter show highest CD 56 positivity. All cases of Colloid and Nodular Goiter were CD56 positive.

In our study there were 3 cases of papillary thyroid carcinoma out of which two cases were conventional papillary thyroid carcinoma and one case was follicular variant of papillary thyroid carcinoma. All three cases of papillary thyroid carcinoma were negative for CD56.

Thus lowest CD56 positivity in papillary thyroid carcinoma.

Table 2: Expression of CD56 in papillary thyroid carcinoma compared to non-papillary thyroid carcinoma thyroid lesions.

Parameter	Papillary Thyroid carcinoma	Thyroid lesions other than Papillary thyroid carcinoma lesion
No of cases	3	52
CD56 negative	3	5
CD56 positive	0	47

In present study, out of 52 thyroid lesions other than papillary thyroid carcinoma lesion forty seven cases were positive for CD56.

Table 3: Statistical analysis of CD56 in present study.

Sensitivity (%)	100%
Specificity (%)	90.38%

In present study CD 56 sensitivity was 100% and specificity was 90.38%.

Discussion

We have observed in this study, CD56 expression was absent in Papillary carcinoma and CD56 expression was retained in majority of benign thyroid lesion.

In present study, there was a positive CD56 immune-expression in all thyroid lesions, except all three PTC cases, all three well differentiated tumor of unknown malignant potential and two cases of adenomatoidgoiter. The sensitivity of CD56 was 100% and specificity was 90.38%. There was one case of FV- PTC which was negative for CD56.Thus CD56 immuno expression has differentiated PTC from Follicular adenoma, Nodular hyperplasia, and Hashimoto Thyroiditis and Follicular thyroid carcinoma.

In Mokhtari et al (2013) total no. of cases was 146, out of which 73 were papillary thyroid carcinoma and 73 were Non PTC thyroid lesions. Out of 73 PTC cases 72 show CD56 negativity and 1 show CD56 positivity.

Out of 73 Non PTC thyroid lesion 70 show CD56 positivity and 3 show CD56 negativity.

Thus in that study, CD56 sensitivity was 98.6% and specificity was 95.8%.

Conclusion:

CD56 is an useful marker for Diagnosis of papillary thyroid carcinoma including the Follicular variant in IHC examination.The absence of CD56 expression in Follicular variant of papillary thyroid carcinoma can be useful in differentiating it from other thyroid nodules with follicular pattern.CD56 expression allowed the differentiation of papillary thyroid carcinoma from non-neoplastic lesions and other thyroid tumor derived from follicular cells with very high sensitivity and specificity.

References

1. Hundal SA, Fleming ID, Fremgen AM, Menck HR. A National Cancer Data Base report on 53,856 cases of thyroid carcinoma treated in the U.S., 1985-1995.Cancer.1998; 83:2638-48.
2. Rosai J, Ackerman LV.Rosai and Ackerman's Surgical Pathology. Elsevier Mosby; 2011; 10th edition, Volume 1:504-514.
3. Carcangiu ML, Zampi G, Pupi A et al. Papillary carcinoma of the thyroid. A clinicopatologic study of 241 cases treated at the University of Florence, Italy.Cancer.1985; 55(4):805-828.
4. Carcangiu ML, Zampi G, RosaiJ. Papillary thyroid carcinoma: a study of its many morphological expressions and clinical correlates. Athol ANNU. 1985; 20(Pt 1):1-44.
5. Asioli S, Erickson LA, Sebo TJ, et al. Papillary thyroid carcinoma with prominent hobnail features: a new aggressive variant of moderately differentiated papillary carcinoma. A clinicopathologic, immunohistochemical, and molecular study of eight cases. Am J Surg Pathol. 2010; 34(1):44-52.
6. Naganuma H, Murayama H, Ohtani N, et al. Optically clear nuclei in papillary carcinoma of the thyroid: demonstration of one of the fixation artifacts and its practical usefulness. Athol Int. 2000; 50(2):113-118.
7. Johannessen JV, Gould VE, Jao W. The fine structure of human thyroid cancer. Hum Pathol. 1978; 9(4):385-400.
8. Batistatou A, Scopa CD. Pathogenesis and diagnostic significance of nuclear grooves in thyroid and other sites. Int J Surg Pathol. 2009; 17(2):107-110.
9. Yamashita T, Hosoda Y, Kameyama K, et al. peculiar nuclear clearing composed of microfilaments in papillary carcinoma of the thyroid. Cancer. 1992; 70(12):2923-2928.
10. Lee TK, Myers RT, Marshall RB, et al. The significance of mitotic rate: a retrospective study of 127 thyroid carcinomas. Hum Athol. 1985; 16(10):1042-1046.
11. Kondo T, Nakazawa T, Murata S, Katoh R. Stromal elastosis in papillary thyroid carcinomas. Hum Pathol.2005; 36(5):474-473.
12. Johannessen JV, Sobrinho-Simoes M. The origin and significance of thyroid psammoma bodies. Lab Invest.1980; 43(3):287-296.
13. Chen KT, Rosai J. Follicular variant of thyroid papillary carcinoma: a clinicopathologic study of six cases. Am J Surg Pathol. 1977; 1(2):123-130.
14. Tielens ET, Sherman SI, Hruban RH, Ladenson PW. Follicular variant of papillary thyroid carcinoma. A clinicopathological study.Cancer.1994; 73(2):424-431.
15. Lindsay S. Carcinoma of the Thyroid Gland: A Clinical and Pathologic study of 293 Patients at the University of

California Hospital. Springfield III: Charles C Thomas: 1960.
16. Liu j, Singh B, Tallini G, et al. Follicular variant of papillary thyroid carcinoma: a clinic pathologic study of a problematic entity. Cancer. 2006; 107(6):1255-1264.
17. Alboves –Saavendra J, Wu J.The many faces and mimics of papillary thyroid carcinoma. Endocrpathol 2006; 17:1-18
18. Eidelman S Damsky CH, Wheelock MJ, DamjanovI. Expression of the cell-cell adhesion glyprotein cell.CAM.120180 in normal human tissues and tumours.AM J. Pathol 1989;135:101-10.
19. VonwasielewskiR, Rhein, Werner M,Sch- eumann GF, DralleH, PotterE. Immunohistochemical detection of E-cadherin in differentiated thyroid carcinomas correlates with clinical outcome cancer 1997;57:2501-7.
20. Mokhtari M., Eftekhari M., Tahririan R., Absent CD56 expression in papillary thyroid carcinoma: A finding of potential diagnostic value in problematic cases of thyroid pathology. Journal of Research in Medical Sciences: The Official Journal of Isfahan University of Medical Sciences, 18(12):1046-1050.
21. Smuthusamy S.,Shah S.A., Suhaimi S.N., Kassim N.,Mahasin M., Saleh M.F.M. and Nurismah MD ISA,CD56 expression in benign and malignant thyroid lesions, Original article, Malaysian J Pathol 2018; 40(2): 111-119.
22. Bancroft J. D; Layton C, Suvarna S.K.(2019). Immunohistochemically and immunofluorescent techniques. Bancroft's theory and practice of histological techniques.8th edition, p.337-394.Pernick N.CD markers, pathology outline, 19 Aug.2019.
23. Smuthusamy S, Shah S.A, Suhaimi S.N, Kassim NM, Saleh M.F.M. and Nurismah MD ISA, CD56 expression in benign and malignant thyroid lesions, Original article, Malaysian J Pathol 2018;40(2):111-119.