Immunohistochemical Expression of Clustered Differentiation 10 (CD10) Across Various Grade & Stage of Urinary Bladder Carcinoma

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Abstract

Objective: To assess the Clustered Differentiation 10 (CD10) expression in Urothelial carcinoma and to ascertain how its expression relates to grade and stage.

Method: Descriptive cross sectional research was carried out over a period of six months in Pathology Department on eighty five cases of bladder carcinoma from transurethral resection of bladder (TURBT) specimens diagnosed on Hematoxylin-eosin (H & E) stained sections irrespective of patient's age and gender were included in the study. These were stained for CD10 by Immunohistochemical technique.

Results: Sixty seven (78.8%) urothelial carcinomas showed positive CD10 staining while 18 cases (21.17%) demonstrated negative expression. In 67 positive cases, 42 high grade tumors had 2+ expression while 13 grade had 1+ staining . All low-grade tumors (12) displayed 1+ score. Sixteen tumors in pT1, 21 tumors in pT2 and 3 tumors in pT3 stage displayed 2+ score. Nineteen tumors in pT1 while 4 tumors in pT2 had 1+ score.

Conclusion: Our findings indicate that CD10 expression is greater in high grade and invasive urothelial carcinomas and is associated with progression of bladder carcinomas.

Keywords: Urothelial carcinoma, Clustered Differentiation 10(CD10), Immunohistochemistry.

How to cite: *Shoukat S, Nabi Uzma, Begum A, Sarwar A, Sadiq S, Irfan F. Immunohistochemical Expression of Clustered Differentiation 10 (CD10) Across Various Grade & Stage of Urinary Bladder Carcinoma. Esculapio - JSIMS 2023;19(02):231-235*

DOI: https://doi.org/10.51273/esc23.2519219

Introduction

Urothelial carcinoma ranks as tenth most prevalent tumor worldwide.[1] In Pakistan, Punjab Cancer Registry reported the percentage of bladder cancer to be 3.2% for the year 2018.[2] Smoking and genetic alterations constitute key factor responsible for development of carcinogenesis.[3] Many genes related to several signaling pathways, undergo mutations over a long period of time.[3] Clustered Differentiation 10(CD10) is a single chain zinc dependent metalloprotease.[4] It is additionally referred to by the names neutral endopeptidase (NEP 24.11), neprilysin and enkephalinase as well as common acute lymphocytic leukemia antigen (CALLA).[5] Pre-B cells, Pre-T cells, germinal centre B cells, granulocytes, uterine connective tissue, myoepithelial cells, fibroblasts, epithelial cells of hepatocytes, renal parenchyma, mammary tissue, adrenal cortex, lung and cells of central nervous system all routinely express CD10.4 Its expression has been demonstrated in many hematopoietic and non-hematopoietic tumors e.g. acute lymphoblastic leukemia, terminal phase of chronic myelogenous leukemia, urinary bladder carcinoma and colon adenocarcinoma.[5] A variety of biologically active peptides are inactivated by CD 10.6 It plays an important role in controlling cell proliferation and death[5]. Additionally, it may induce carcinogenesis by neoplastic transformation in cells lining the urinary bladder[7]. By changing the cellular microenvironment, it is believed to have an impact on invasion into the underlying tissue as well enhancing the capacity of these malignant cells to spread to distant sites.[7] The purpose of this study is to evaluate

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Submission Date: 16-04-2023
1st Revision Date: 06-05-2023
Acceptance Date: 02-06-2023

the expression of CD10 in relation to grade and stage of tumor. Expression of CD10 has not been recently evaluated in Pakistan, even though urothelial carcinoma is commonly encountered in our practice. Hence this study will help to compare our local population data with the international ones.

Material and Method

This research was carried out in Pathology Department of Tertiary care Hospital (IRB Reference No. 39122) for six months. Eighty five cases diagnosed cases of urinary bladder malignancy irrespective of gender, degree of differentiation and pathological stage received via Transurethral resection of bladder (TURBT) were selected by Non-Probability, consecutive sampling technique were included in the study. Poorly fixed specimens and specimens with scant tumor tissue and those diagnosed either as adenocarcinoma, sarcoma, lymphoma or metastatic carcinoma carcinoma on microscopic evaluation were excluded from the study. Tumors were categorized depending upon their degree of differentiation as per WHO guidelines. For histopathological staging purposes, AJCC staging 8th edition was employed on these TURBT specimen.

IHC results were interpreted on light microscopy using high power field objective. Cell membrane and or cytoplasmic staining was considered positive pattern[7]. Healthy renal tissue served as the positive control for the CD10 specificity. Cells of both glomeruli and tubules exhibited brown membranous and cytoplasmic staining, which was indicative of positive[7]. Depending on the proportion of positive cells stained for CD10, scoring was carried out as follows:

- Negative 0 (< 5% membranous or cytoplasmic staining of cells)
- Positive 1+ (>5 - 50% membranous or cytoplasmic staining of cells)
- Positive 2+ (>50% membranous or cytoplasmic staining of cells)

In order to evaluate the data, SPSS version 20.0 was utilized. Findings were expressed as percentages. The post-stratification chi-square test was performed, with a p value of 0.05 accepted as significant.

Results

The recruited cases were between the ages of 40 and 90, with a mean age of 63.96 10.13 years (Figure I).Out of 85 cases, 77 (90.59%) were men and 8 (9.41%) were women resulting in male to female ratio of 9.6:1. Regarding histological grade, 57(67.1%) were high grade while 28(32.9%) had low grade morphology. Regarding pathological staging, 9 (10.6%) were in pTa stage, 5 (5.9%) belonged to pTis, 43 (50.6%) in pT1, 25 (29.4%) in pT2 while 3 (3.5%) in pT3 . Among 85 cases, 67 cases (78.8%) demonstrated positive staining while 18 cases (21.17%) exhibited negative staining for CD10 (Table 1).

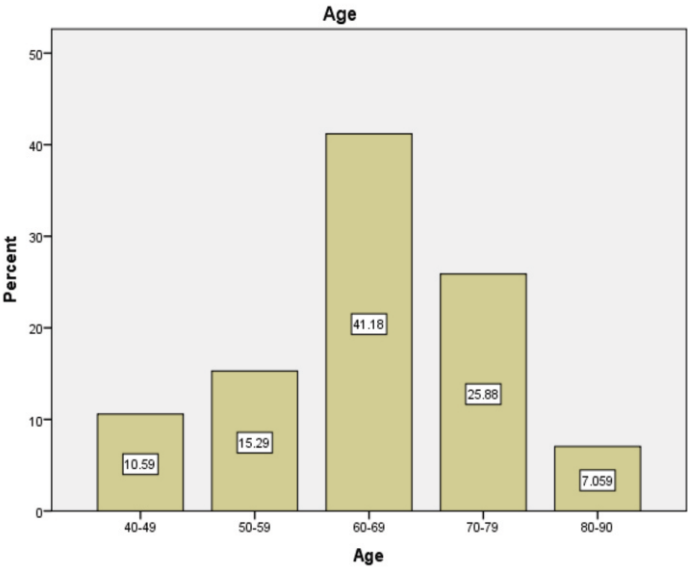


Figure I: *Distribution of cases according to Age groups (n=85)*

Figure II: Non- invasive urothelial carcinoma (pTa) (1+ CD10 immunostain at 40x)

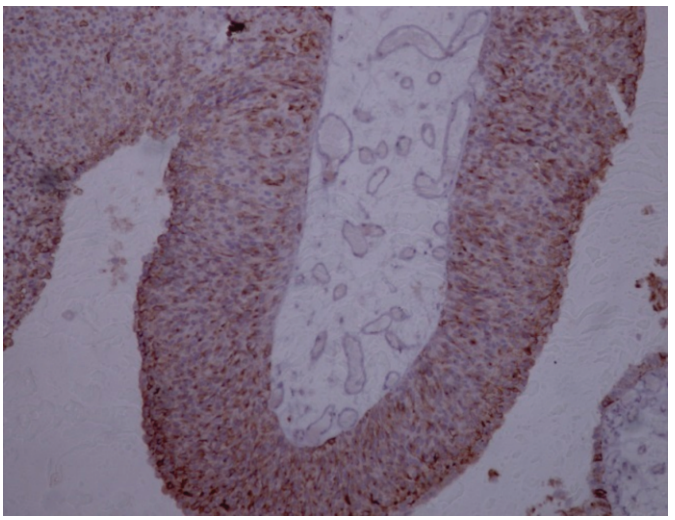


Figure 2: *Invasive (pT1) High grade urothelial carcinoma (2+CD10 immunostain at 40x)*

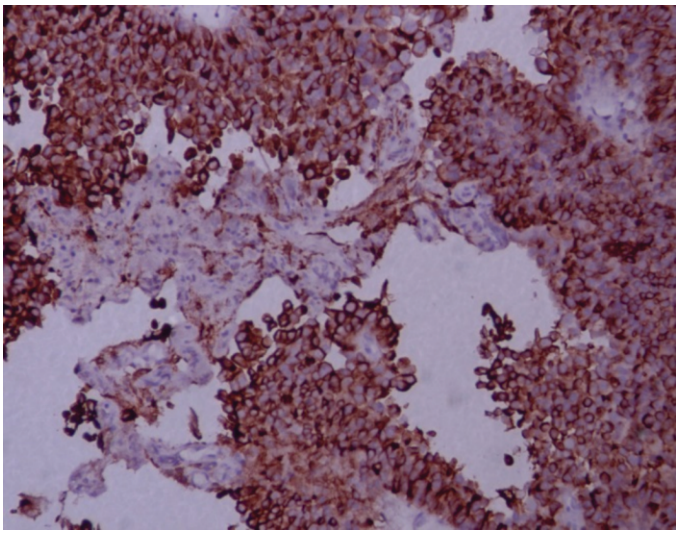
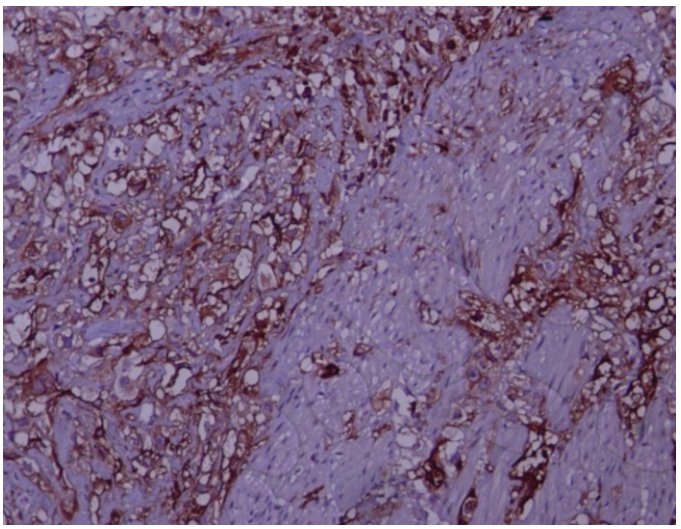


Figure 3: *Invasive (pT2) High grade urothelial carcinoma (2+CD10 immunostain at 40x)*



Discussion

Urothelial carcinoma of bladder is the 10th most frequent and 8th most fatal cancer primarily affecting males[8]. It is an insidious malignancy that killed close to 20,0000 globally in 2018 alone. As per the data compiled by Globocan and published in 2019, Bray et al calculated the numbers of reported new bladder cancers to be at 549,393 in the world, constituting 3% of the total cancer disease burden for the year 2018.[9] Although most of the bladder tumors are confined to the mucosa at the time of diagnosis but a significant percentage of tumors are advanced and muscle infiltrative.[10] According to Cancer Facts & Figures 2020 published by American Cancer Society, mortality due to bladder cancer remains higher among men.[11] Higher mortality can be attributed to diagnostic challenges resulting in delay in diagnosis and higher stage of disease at the time of presentation.[12]

Table 1: *Stratification of CD10 immunoexpression with respect to Grade and Stage of tumor*

Histological Grade	CD 10 Expression		Total = n	p-value
	1+	2+		
Low Grade	12 (17.9%)	0 (0%)	28 (17.9%)	
				< 0.001
High Grade	13 (19.4%)	42 (62.6%)	57 (82.1%)	
Pathological Stage	**CD 10 Expression**		**Total = n**	**p-value**
	1+	**2+**		
PTa	2 (2.9%)	2 (2.9%)	4 (5.9%)	
pT1	19 (28.3%)	16 (23.8%)	35 (52.2%)	
pT2	4 (31.3%)	21(31.3%)	25 (37.3%)	***< 0.001***
pT3	0 (0%)	3 (4.4%)	3 (4.4%)	

In our study, CD10 positivity was seen in 78.82% with positive correlation with histological grade and pathological stage. 2+ positivity was seen in 42 while 1+ reaction was visualized in 13 high grade tumors. 1+ positivity was present in each of the 12 low grade carcinomas. With a p-value < 0.001, the association between CD10 and tumor grade is highly significant (Table 1). These findings concurred with those of the study conducted in Egypt.[12] With a p value 0.001, the association between CD10 expression and tumour stage for urothelial carcinomas is likewise statistically noteworthy (Table 1). CD10 expression was seen in 4 out of 9 pTa tumor , 35 out of 43 in pT1, 25 pT2 and 3 pT3 tumors. While none of the five tumors in pTis revealed any positive expression. Additionally, Atique et al.[13], Shukla et al,[14] Muhammad et al.[15], and Asmaa Hussein et[12] noted this apparent relationship to stage. A substantial correlation between CD10 staining and tumour grade was seen after stratifying the data. Out of 57 high grade tumors, 42 displayed +2 and 13 exhibited +1 staining. Contrarily, none of the 28 low grade tumors displayed +2 staining, 12 revealed +1 staining, and 16 did not exhibit any expression. Having p-value <0.001, the link between CD10 expression and carcinoma grade is of statistical importance (Table I). These results coincided with the one research.[11] When data was stratified for stage, similar direct association of CD10 expression was observed. While 24 out of 28 pT2 carcinomas demonstrated +2 staining, mere 16 out of 43 pT1 carcinomas did so. With a p-value < 0.001, the connection

involving CD10 expression with tumour stage is noteworthy as well (Table I).This close association with both grade and stage was also observed by Atique et al,[12] Shukla et al,[13] Muhamed et al9 and Asmaa Hussein et al.[11] In 2000, Chu and Arber16 reported CD10 positivity in 54% of urothelial carcinomas. Murali conducted the first study on the relationship between CD10 expression and tumour grade or stage in 2005.He concluded that high grade urothelial neoplasms express strong CD10 positivity.[17] He came to numerous conclusions about the role of CD10 in carcinogenesis, one of which was that the buildup of mutant, nonfunctional CD10 may be the root cause of elevated CD10 expression.

Shukla et al.[13] also came to the conclusion that there is a strong relationship between CD10 with degree of differentiation, stage, and longevity in patients hence establishing its role in prognosis.

Conclusion

CD10 expression advances with increasing grade and stage. This raises the possibility that CD10 has a role in the onset and progression of urothelial carcinoma, which can be studied more thoroughly in order to develop a molecular customized therapy. More comprehensive studies with a longer follow-up period would be beneficial to examine CD10's efficacy in patient management and determine its precise significance as a prognostic marker in bladder malignancy.

Conflict of Interest *None*

Funding source *None*

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Authors Contribution

UR, SS: Conceptualization of Project
SS, SS: Data Collection
FI, SS: Literature Search
AB, AS: Statistical Analysis
UR, AB, AS: Drafting, Revision
AS, AB: Writing of Manuscript