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Original Research Article

Study of CD10 Expression in Urothelial Carcinoma of Bladder

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Conflict of interest: Nil

Abstract

Background: Urothelial carcinoma represents the second most frequent malignancy of the genitourinary tract following prostate, with rising incidence. CD10 is a single-chain, 90-110 kDa cell surface zinc dependent enzyme metalloprotease. It is expressed by both normal and neoplastic haematopoietic cells and also in a variety of non haematopoietic tissues and neoplasms.

Aim: To compare CD10 expression in various grades and stages of urothelial carcinoma.

Methods: A two years cross-sectional study was carried out on urothelial carcinoma in the department of pathology, RIMS, Imphal for the period September 2017 to August 2019. A total of 30 cases of histologically confirmed urothelial carcinomas were included in the study. All cases were evaluated histopathologically, graded according to the WHO/ISUP 2004 classification and pathological staging was done according to TNM system. Immunostaining with immunohistochemical marker CD10 was done for all the cases and a semi-quantitative scoring was performed based on percentage of positive cells.

Results: Out of total 30 cases, 18 (60%) were low grade and 12 (40%) were high grade papillary urothelial carcinoma. Of all the cases, 21 (70%) showed positive CD10 immunostaining while 9 (30%) were negative. Rate of CD10 positivity was increased significantly in higher grade of tumors (p-value 0.049) and higher pathological stage of tumors (p-value 0.009). The degree of expression of CD10 immunostaining score (scale 0-2) was also increased significantly with the higher grade of tumors.

Conclusion: Our findings indicate that CD10 expression is strongly correlated with high tumor grade and stage in urothelial carcinoma of the bladder. CD10 may be associated with tumor invasion and metastasis in bladder cancer pathogenesis.

Keywords: Urinary bladder, Neoplasm, Grade, Stage, CD10.

Introduction

Urinary bladder cancers accounts for approximately 7% of cancer and 3% of cancer mortality in USA. About 95% bladder tumors are originates from epithelium and the rest are from mesenchyme. Most epithelial tumors (90%) are of urothelial/transitional cell type and are called Urothelial/Transitional tumors. [1] As per the Indian cancer registry data in men, it is the ninth most common cancer accounting for 3.9% of all cancer cases in India.[2] Urothelial carcinoma most commonly presents over the age of 50 years and about 80% patients are between 50-80 years of age but can also be seen in younger adults and children. Incidence of the disease and mortality from the disease increases further with age. Males are nearly three times more commonly affected than females. Whites are affected more than the blacks. Cigarette smoking causes three to seven fold increased risk of developing urothelial carcinoma. The risk correlates with the number of cigarettes smoked, the duration of smoking and the degree of inhalation of smoke. Smoke contains aromatic amines and polycyclic aromatic hydrocarbons which are excreated through kidney. Industrial exposure to aryl amines (2-naphthylamine and related products), aniline dye, combustion gas & soot from coal, chlorinated aliphatic hydrocarbons, certain aldehydes such as acrolein (used in chemical dyes, in rubber and textile industries) are associated with increased risk of developing urothelial carcinoma. Long term use of analgesic containing Phenacetin, an active metabolite of Acetaminophen can increases risk of bladder cancer. Chronic cystitis due to indwelling catheter or calculi and *Schistosoma haematobium* induced cystitis appears to be causally related to the development of bladder cancer. Acrolein, an urinary metabolite of Cyclophosphamide is

believed to be responsible for both hemorrhagic cystitis and bladder cancer. Cyclophosphamide used for long time have upto nine fold increase of bladder cancer and the latent period of developing cancer ranges from six to thirteen years. There is slight increase risk of bladder cancer in patients who are given pelvic irradiation for other pelvic malignancies. Coffee and tea drinking, artificial sweeteners, low fluid intake are also thought to cause bladder cancer.[1-4]

More than 90% of urinary bladder cancers are urothelial carcinoma (TCC), where as primary squamous cell carcinoma (SCC), small cell carcinoma, adenocarcinoma and other tumors are less common.[5]

CD10 is a single-chain, 90-110-kDa cell surface zinc dependent enzyme metalloprotease. It inactivates various bioactive neuropeptides. CD10 is synonymous with common acute lymphocytic leukaemia antigen(CALLA), enkephalinase, membrane metalloendopeptidase (MME), membrane-associated neutral endopeptidase and neprilysin.[8,9,19,11] CD10 is expressed on the surface of a variety of both normal and neoplastic haematopoietic and lymphoid cells.[12] CD10 plays important roles in maintenance of homeostasis, neoplastic transformation and tumour progression.[13] It was initially discovered on the surface of acute lymphoblastic leukaemia cells and was considered to be a tumor-specific antigen.[14] CD10 can be found in different normal cells including cells of non-hematopoietic origin such as glomerular and proximal tubular epithelium of the kidney, liver, breast myoepithelium, lung, fibroblasts etc. Cells of the central nervous system are able to express CD10. It is also expressed by a number of hematopoietic cells such as immature T and B cells, B cells of the germinal centre of lymphoid follicles, and granulocytes as well as lymphoid malignancies including the majority of acute lymphoblastic leukaemia, and also follicular centre lymphoma, lymphoblastic, Burkitt's, and nodular poorly differentiated lymphocytic lymphomas, and chronic myelogenous leukaemia in lymphoid blast crisis. CD10 expression has been reported in many non-hematopoietic neoplasms like renal cell carcinoma, endometrial stromal tumor, solid and pseudopapillary tumor of the pancreas, melanoma, carcinoma of the prostate, breast, stomach, and colon. [9-16] CD10 protein also has direct role in signal transduction pathways which regulate cell growth and apoptosis. It is thought that due to its structural similarity to the matrix metalloproteases in the stroma, CD10 also affects the invasion and metastatic potential of tumor cells by altering the cellular microenvironment. CD10 expression in intra-tumoral stromal cells may also contribute to tumor progression.[12,19]

Bircan S et al [17] found 9.1% non-tumoral cases positive for CD10 immunostaining. Murali R et al [30] demonstrated CD10 staining in 50 % non-neoplastic urothelium. Its expression has been reported to occur in 43%–67% of urothelial neoplasms. While in the majority of reports, CD10 expression shows an inverse correlation with tumor grade, a positive correlation with grade has been noted in others.[17-19] Many studies were done to compare CD10 expression with relation to various grades and stages of urothelial carcinoma and found that it's expression was greater in high grade and invasive urothelial carcinomas. [6,8,14,17,19]

To the best of our knowledge, only a few studies conducted till date and evaluated CD10 IHC expression in urothelial carcinoma of urinary bladder. In the present study we have attempted to identify the correlation, if any, between CD10 expression and histopathological parameters including grade and stage. Subsequently, we sought to determine whether CD10 IHC expression could have a prognostic value in the assessment of urothelial carcinoma.

Aim and Object

To compare CD10 expression with relation to various grades and stages of urothelial carcinoma.

Materials and Methods

A two years (September 2017 to August 2019) cross-sectional study was carried out in the department of pathology, in collaboration with department of Urology, RIMS, Imphal

Patients whose TURB (transuretheral resection of bladder tumor) and cystectomy specimens were sent for histopathological examination and subsequently diagnosed as Urothelial carcinoma of bladder were included in this study.

Patient with Urothelial carcinoma who was being treated with or was treated with chemotherapy and/or radiotherapy, inadequate sample and those who have not given consent for the study were excluded from this study

Sample size

Sample size was calculated based on the formula:

$$N = \frac{Z^2PQ}{L^2} = \frac{(1.96)^2 \times 3.9 \times 96.1}{8^2} = \frac{1439.79}{64} = 22.49 \cong 23$$

Where

Z=1.96 (at 95% confidence interval)
P = prevalence of urothelial carcinoma 3.9 % in India (as per Indian cancer registry data).[2]
Q= (100-P); L = absolute allowable error (8 %)

The calculate sample size was 23. However, we have included all urothelial carcinoma cases during the study period, as per inclusion and exclusion

criteria of this study. Study variables comprising of (a) independent variables:- age and sex of the patients and (b) dependent variables:- histopathological diagnosis (grade and stage of urothelial carcinoma), CD10 expression (positive, negative, immunostaining score) Haematoxylin and eosin stained sections all cases were evaluated histopathologically, graded according to the WHO/ISUP 2004 classification [13, 6]. Pathological staging was done according to TNM system (7th edition). [14, 7] For CD10 immunohistochemistry standard protocol was followed. CD10 staining cases showing focal or patchy brown stains in intra-cytoplasm and/or cell membrane of urothelial carcinoma cells after staining with IHC marker and visualized under light microscope was considered as positive cases for CD10 in urothelial carcinoma cells.

Scoring system

The proliferative index program was used to obtain the percentage of positive immune-stained cells; a mean of 500 cell count was performed in each case at high power after selecting the highest staining areas at low power.

% of positive cells =

$$\frac{\text{Number of positive cells} \times 100}{\text{Total number of counted cells}}$$

The staining density was scored semi-quantitatively based on the percentage of positive cells performed according to the following staining criteria:

Table 1:

Score	Pattern
Negative (0)	< 5% positive cells
1+	5%-50% positive cells
2+	>50% positive cells

Control

Positive control → Tonsil
Negative control → Normal transitional epithelium of prostatic urethra or urinary bladder.

Data Collection

Brief clinical information with regards to age, sex, race, etc. of the patient and clinical data received from the case files of the patient were recorded in the proforma prepared for the study. Samples were processed as per the guidelines of inclusion and exclusion criteria.

Statistical Analysis

Data entry and analysis was done using SPSS Version 21. Mean, standard deviation, percentage and proportion were used for descriptive statistics. Fisher's exact test was used to find the association between relevant outcome variables and some selective variables of interest. *P*-value of < 0.05 was considered as statistically significant.

Ethical Issues

Ethical approval was obtained from the Research Ethics Board (REB), RIMS, Imphal with registration number A/206/REB-Comm (SP)/RIMS/2015/ 309/52/2017. Permission for the study in Manipur University, Vice Chancellor, before the beginning of the study was obtained. Informed verbal consents were obtained from the respondents.

A code number was assigned and no names were taken to maintain confidentiality and privacy. Data collected were kept secured.

Results and Observation

During the study period, as per inclusion and exclusion criteria of this study, a total of 30 specimens (4- cystectomy, 26 -TURBT) were included in the study. Histological examination and CD10 immunohistochemical analysis of all the specimens were done.

Clinicopathological Characteristics

The age ranged from 42 years to 88 years and mean age of study population was 65.63 ± 11.82 SD. The commonest age group was seen in 61-70 years (43.3%) followed by 71-80 years (23.3%) and 41-50 years (23.3%) (Figure no. 1).

Among the 30 cases, 27 (90%) were male and 3 (10%) were female with a male to female ratio of 9:1.

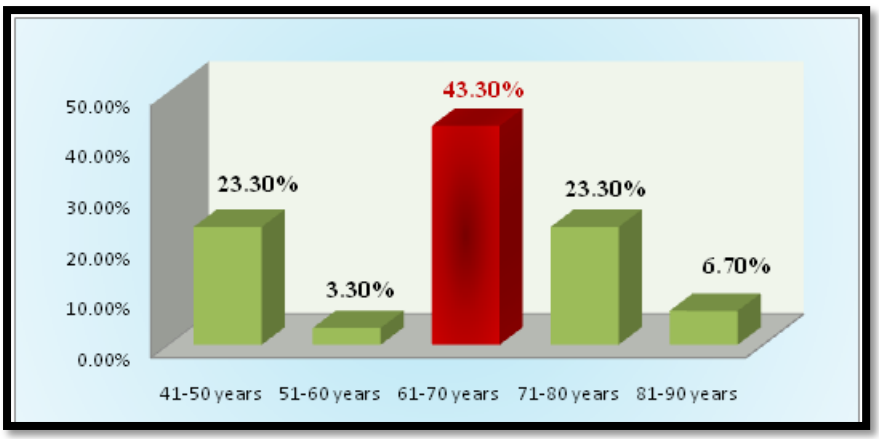

Figure 1: Bar diagram showing distribution of all cases according to age group

According to the WHO/ISUP (2004) grading system of urothelial carcinoma of bladder, among the 30 cases, 18 (60%) cases were low grade papillary urothelial carcinoma and 12 (40%) were high grade papillary urothelial carcinoma. However, no case of papillary urothelial neoplasm of low malignant potential was detected in our study.

Table 2: Overall distribution of urothelial carcinoma according to pathological stage

Grade	Stage			Total
	pT_a	pT_1	pT_{2-4}	
Low grade papillary urothelial carcinoma	8 (44.4%)	8 (44.4%)	2 (11.1%)	18 (100.0%)
High grade papillary urothelial carcinoma	2 (16.7%)	4 (33.3%)	6 (50.0%)	12 (100.0%)
Total	10 (33.3%)	12 (40.0%)	8 (26.7%)	30 (100.0%)

Table no. 2 shows that according to pathological staging (TNM staging, 7th Edition), the distribution of urothelial carcinoma was 10 (33.3%), 12 (40.0%) and 8 (26.7%) in stage pT_a, stage pT_1 and stage pT_{2-4} respectively.

Table 3: distribution of urothelial carcinoma according to invasiveness

Grade	Invasive	Non-invasive	Total
Low grade papillary urothelial carcinoma	10 (55.6%)	8 (44.4%)	18 (100%))
High grade papillary urothelial carcinoma	10 (83.3%)	2 (16.7%)	12 (100%))
Total	20 (66.7%)	10 (33.3%)	30 (100%)

Table no. 3 shows that 55.6% (11/18) of low grade tumors and 66.7% (10/12) of high grade tumours in our study are invasive in nature.

Bladder cancer also classified as non-muscle invasive bladder cancer (NMIBC, superficial) and muscle invasive bladder cancer (MIBC). Table no. 3 shows that 11.1% (2/18) of low grade tumours and 50.0% (6/12) of high grade tumours shows muscle invasion.

Table 4: Distribution of urothelial carcinoma according to muscle invasion

Grade	Muscle invasion		Total
	MIBC	NMIBC	
Low grade	2 (11.1%)	16 (88.9%)	18 (100.0%)
High grade	6 (50.0%)	6 (50.0%)	12 (100.0%)
Total	8 (26.7%)	22 (26.7%)	30 (100.0%)

Immunohistochemical findings

Out of total 30 cases of urothelial carcinoma 21 (70%) showed positive (+1 & +2) CD10 immunostaining while 9 (30%) were negative. Predominant CD10 immunostaining pattern was cytoplasmic and less commonly we found combined cytoplasmic and membranous pattern also.

Table 5: Overall CD10 expression according to histological grade

Grade	CD10 immunostaining		Total	p – value (Fisher's Exact Test)	Remark
	Positive (score- +1,+2)	Negative (score- 0)			
Low grade	10(55.6%)	8(44.4%)	18(100%)	0.049	Significant
High grade	11(91.7%)	1(8.3%)	12(100%)		
Total	21(70.0%)	9(30.0%)	30(100%)		

Table no 5 shows that of the 18 cases of low grade papillary urothelial carcinoma, 10 (55.6%) showed positive CD10 immunostaining and 8 (44.4%) were negative whereas of the 12 cases of high grade papillary urothelial carcinomas 11 (91.7%) were positive and only 1 (8.3%) was negative. These findings suggest that rate of CD10 positivity increased significantly in higher histological grade of tumors (p-value 0.049).

Table 6: Overall CD10 expression according to pathological stage

Stage	CD10 immunostaining		Total	p – value (Fisher's Exact Test)	Remark
	Positive (score- +1,+2)	Negative (score- 0)			
pT_a	4(40.0%)	6(60.0%)	10(100.0%)	0.034	Significant
pT_1	11(91.7%)	1(8.3%)	12(100.0%)		
pT_{2-4}	6(75.0%)	2(25.0%)	8(100.0%)		
Total	21(70.0%)	9(30.0%)	30(100.0%)		

Table no. 6 shows that according to stage, the positive rate of CD10 expression was 4/10 (40.0%) in stage pT_a, 11/12 (91.7%) in stage pT_1 and 6/8 (75.0%) in stage pT_{2-4}, this suggests that CD10 positivity increased significantly in higher pathological stage of tumor as compared to pT_a (p-value 0.009). Table no. 7 shows that predominant CD10 immunostaining score in low grade tumors was +1 (ie. focal) whereas in high grade it was + 2 score (ie. diffuse). Degree of expression of CD10 immunostaining score (scale 0-2) was increased significantly with the higher pathological grade of tumor. However we did not find any significant correlation between degree of expression of CD10 immunostaining score and pathological stage (p-value 0.210) (Table no. 8).

Table 7: Immunostaining Score of CD10 according to pathological grade

Grade	CD10 immunostaining Score			Total	p – value (Fisher's Exact Test)	Remark
	0	+1	+2			
Low grade	6 (33.3%)	10 (55.6%)	2 (11.1%)	18 (100%)	0.009	Significant
High grade	1 (8.3%)	3 (25.0%)	8 (66.7%)	12 (100%)		
Total	7 (23.3%)	13 (43.3%)	10 (33.3%)	30 (100%)		

Table 8: Immunostaining score of CD10 according to pathological stage

Stage	CD10 immunostaining score			total	p – value (Fisher's Exact Test)	Remark
	0	+1	+2			
pT_a	5 (50.0%)	3 (30.0%)	2 (20.0%)	10 (100%)	0.210	Insignificant
pT_1	1 (8.3%)	7 (58.3%)	4 (33.3%)	12 (100%)		
pT_{2-4}	1 (12.5%)	3 (37.5%)	4 (50.0%)	8 (100%)		
Total	7 (23.3%)	13 (43.3%)	10 (33.3%)	30 (100%)		

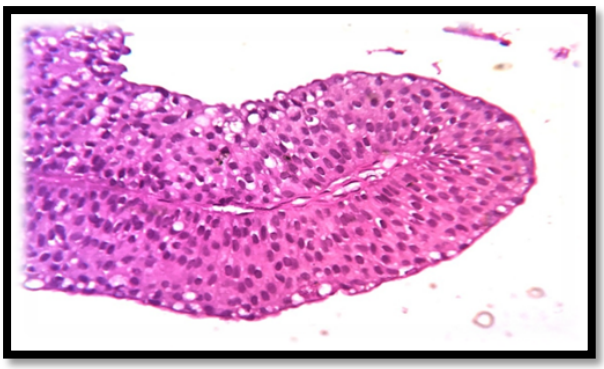

Figure 2 : Photomicrograph of low grade papillary urothelial carcinoma (H&E,400x)

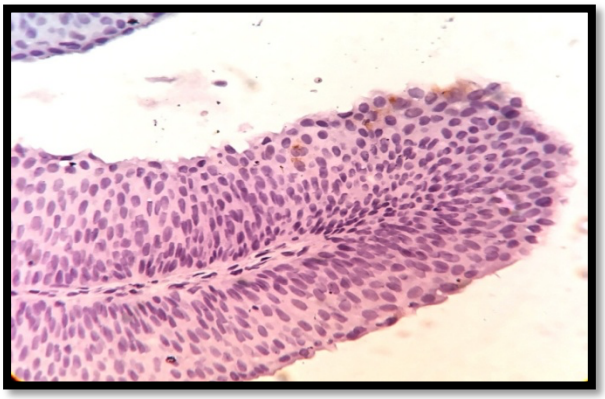

Figure 3: Photomicrograph of low grade papillary urothelial carcinoma showing CD10 negativity (Score-0) in corresponding section (400x, CD10 IHC stain,Dako)

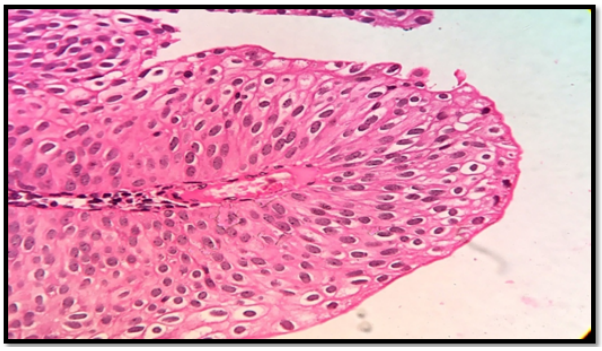

Figure 4: Photomicrograph of low grade papillary urothelial carcinoma (H&E,400x)

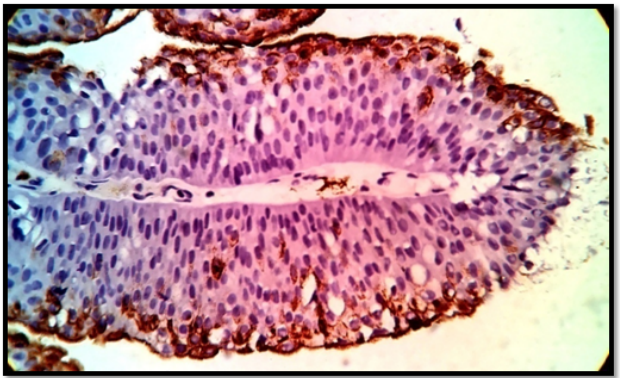

Figure 5: Photomicrograph of low grade papillary urothelial carcinoma showing focal CD10 focal positivity (Score-1) in corresponding section (400x, CD10 IHC stain,Dako)

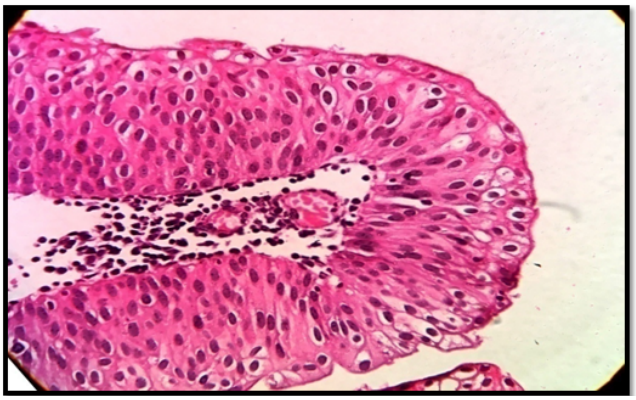

Figure 6: Photomicrograph of low grade papillary urothelial carcinoma (H&E,400x)

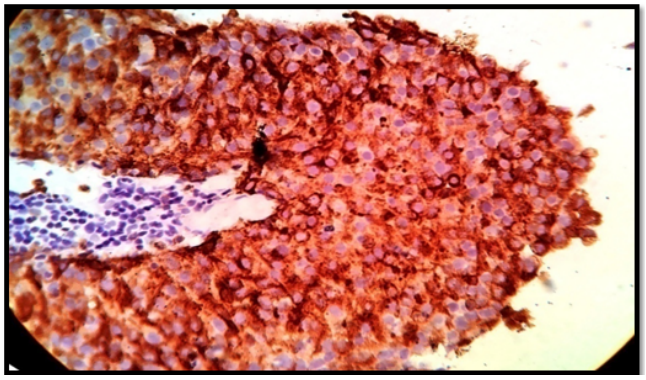

Figure 7: Photomicrograph of low grade papillary urothelial carcinoma showing diffuse CD10 positivity (Score-2) in corresponding section (400x, CD10 IHC stain,Dako)

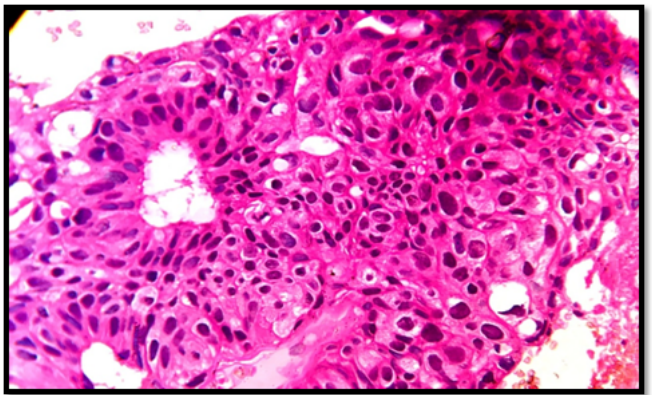

Figure 8: Photomicrograph of high grade papillary urothelial carcinoma (H&E,400x)

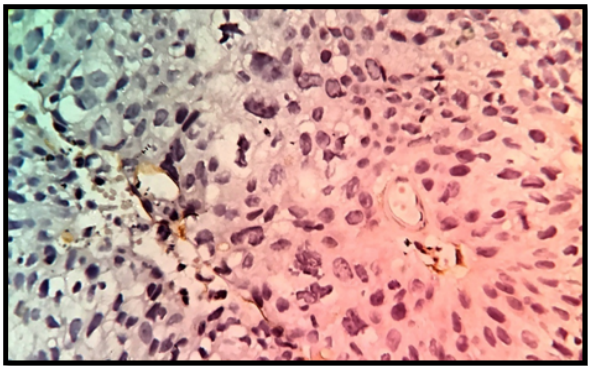

Figure 9: Photomicrograph of high grade papillary urothelial carcinoma showing CD10 negativity (Score-0) in corresponding section (400x, CD10 IHC stain,Dako)

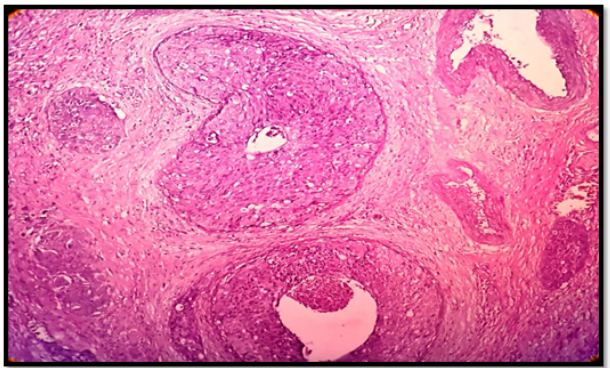

Figure 10: Photomicrograph of high grade papillary urothelial carcinoma (H&E,100x)

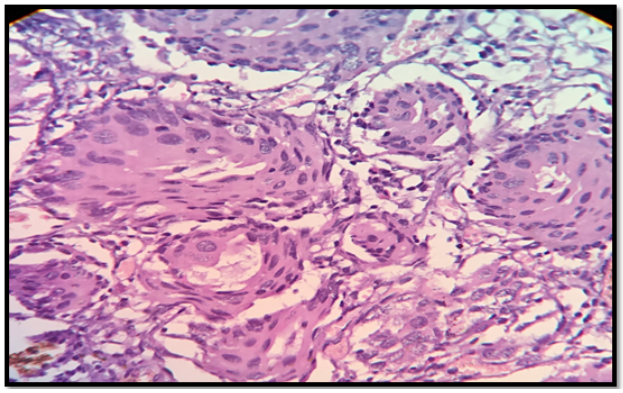

Figure 11: Photomicrograph of high grade papillary urothelial carcinoma (H&E,400x)

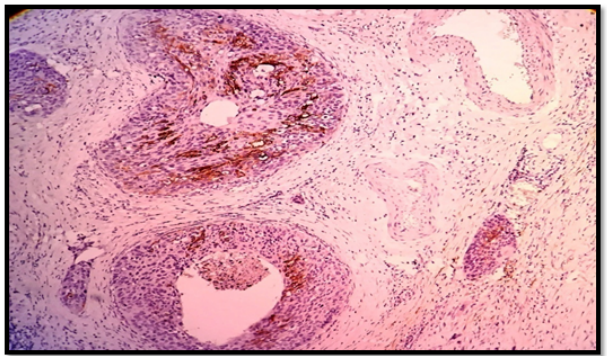

Figure 12: Photomicrograph of high grade papillary urothelial carcinomashowing focal CD10 positivity (Score-1) in corresponding section (100x, CD10 IHC stain,Dako)

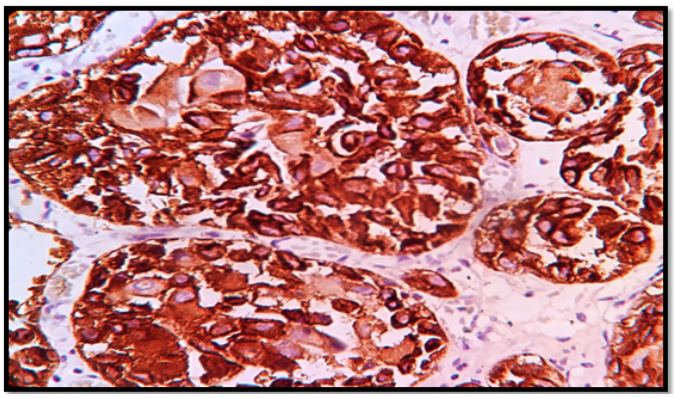

Figure 13: Photomicrograph of high grade papillary urothelial carcinoma showing diffuse CD10 positivity (Score-2) in corresponding section (400x, CD10 IHC stain,Dako)

Discussion

The present study on expression of CD10 in urothelial carcinoma was carried out in 30 patients in the department of pathology in collaboration with department of Urology, RIMS, Imphal.

Age and sex

In this study, the age of the patients ranges from 42 years to 88 years and the mean age of study population was 65.63 ± 11.82 SD. Similar findings were observed by Bircan S et al [17], Bahadir B et al [19], Koyuncuer A [20], Gupta P et al [23], Kandemir NO et al [29] and Samah SS et al [32] where mean age of patients were 55.8 ±13.5 years, 61.36 ± 9.74 years, 56.96 ± 12.1 years, 60.2 ± 4.4 years, 67.2 ± 12.1 years and 61.4 ± 9.7 years respectively.

It was observed that most of the urothelial carcinomas in our study were in the age group of 61-70 years which was consistent with the studies conducted by Laishram RS et al [2], Koyuncuer A [20], Waihenya CG et al [22] and Mylsamy S and Kanakasabapathi D.[24]

In our study, out of the total 30 cases, 27 (90%) were male and 3 (10%) were female with a male to female ratio of 9:1. So as per our study, urothelial carcinoma was 9 times more common in male than in female gender. Similar results were also found by Atique M et al [8], Bahadir B et al [19], Koyuncuer A [20], Gupta P et al [23], Cheng L et al [25] and Samah SS et al [31] where male to female ratio were 9:1, 8:1, 9.4:1,8.6:1, 6:1 and 8:1 respectively. In contrast, Laishram RS et al [4], Waihenya CG et al [39] and Mylsamy S and Kanakasabapathi D [24] in their study, found a lesser male to female ratio which were 1.5:1, 4:1 and 3.6:1 respectively.

Grade

In our study, among the 30 cases, 18 (60 %) cases were low grade papillary urothelial carcinoma which was most common and 12 (40%) were high grade papillary urothelial carcinoma. However, no case of papillary urothelial neoplasm of low malignant potential (PUNLMP) was detected in our study.

Laishram RS et al [2] in their study in 26 cases of urothelial carcinoma found that most common lesion was low grade papillary urothelial carcinoma (53.85%) followed by high grade papillary urothelial carcinoma (34.6%), papillomas (7.7%) and PUNLMP (3.9%) which was almost similar with our findings**.**

Various other studies conducted by Bahadir B et al [19] (59.8%), Koyuncuer A [20] (68%), Matalka I et al [21] (60%) and Biswas RR et al [26] (58%) were also in agreement with our study that low grade urothelial carcinoma was the predominant lesion compared to other histological grades.

In contrast, most common lesions observed by Kandemir NO et al [29] was high-grade urothelial carcinoma (54%) followed by low-grade urothelial carcinoma (46%).

Stage

According to pathological staging, the distribution of urothelial carcinoma in our study was 10 (33.3%), 12 (40.0%) and 8 (26.7%) in stage pT_a, stage pT_1 and stage pT_{2-4} respectively. Here most of the lesions were found in stage pT_1. Similar findings were observed in the study conducted by Bircan S et al.[17] However, this findings were not consistent with the studies conducted by Bahadir B et al [19], Kandemir NO et al [29] and Samah SS et al [31] who found that commonest pathological stage was pT_a.

CD10 expression

In our study, out of total 30 cases of urothelial carcinoma 21 (70%) showed positive (+1 & +2) CD10 immunostaining while 9 (30%) were negative. The above findings were consistent with the studies conducted by Atique M et al [8] (80%), Mohamed AH et al [28] (63.3%) and Kandemir NO et al [29] (70%) where positive CD10 expression was observed in more number of cases. However other studies conducted by Bircan S et al [17] (43%), Bahadir B et al [19] (42.3%), Samah SS et al [31] (47.4%) and Jang JT [32] (23%) tend to differ in their observation of CD10 expression positivity.

Predominant CD10 immunostaining pattern in this study was cytoplasmic and less commonly we found combined cytoplasmic and membranous pattern also. This finding was in agreement with the studies conducted by Bahadir B et al [19], Kandemir NO et al [29], Samah SS et al [31] and Jang JT [32].

In our study, according to histological grade, a positive rate of CD10 immunoreactivity was detected in 55.6 % (10/18) of low grade papillary urothelial carcinoma and 91.7% (11/12) of high grade papillary urothelial carcinoma. These findings suggest that rate of CD10 positivity increased significantly in higher histological grade of tumor (p-value 0.049). Similar results were obtained by Atique M et al [8], Murali R et al [18], Bahadir B et al [19], Mohamed AH et al [28], Kandemir NO et al [29] and Samah SS et al [31]. However our findings were not consistent with other studies conducted by Bircan S et al [17] and Koiso K et al [27] who did not found any significant relationship between CD10 expression and histological grade.

According to stage, the positive rate of CD10 expression in our study was 40.0% (4/10) in stage pTa, 91.7% (11/12) in stage pT1 and 75.0% (6/8) in stage pT2-4. CD10 positivity increased

significantly in higher pathological stage of tumor (p-value 0.009). This finding was in agreement with the studies done by Atique M et al [8], Bahadir B et al[19], Abdou AG [30] and Samah SS et al [31] while not consistent with other study done by Kandemir NO et al [29] who did not found significant correlation between CD10 immunohistochemical expression and pathological stage of urothelial carcinoma. Bircan S et al [17] in their study observed that there was a significant inverse correlation between pathological stages and CD10 immunoreactivity which was also not consistent with our study and they proposed that the higher level of CD10 expression in non-invasive carcinomas appears to inhibit cell invasion. Koiso K et al [27] who was the first to assess the CD10 activity of bladder, found that both enzyme activity and IHC expression were higher in superficial cancers than invasive cancers and normal urothelium which was not consistent with our study and they concluded that CD10 was expressed at a certain stage of differentiation in the course of neoplastic process.

We also observed that the degree of expression of CD10 immunostaining score (scale 0-2) was increased significantly with the higher pathological grade of tumor (p-value 0.009). However we did not find any significant correlation between degree of expression of CD10 immunostaining score and pathological stage (p-value 0.210). A progressive increase in the immunostaining score of CD10 along with an increase in tumor grade suggests that upregulation in antigen expression may occur in higher grade and stage of tumors. Our study was in agreement with the studies done by Atique M et al8, Bahadir B et al [19], Abdou AG [30] and Samah SS et al [31] and not correlating with the other study done by Bircan S et al [17]. However, in contrast no significant association between CD10 IHC score and pathological grade or stage was found by Kandemir NO et al.[29]

Several possibilities may be there regarding the role of CD10 in urothelial tumorigenesis. First, as CD10 is a cell surface metalloprotease, it has the ability to hydrolyze endothelin and thus it might have a role in urothelial angiogenesis by modulating endothelin levels that facilitates cancer cell invasion and metastasis. Probably it is the most acceptable explanation for the significant correlation of CD10 expression with the grade and stage of tumor in this study. Second, as a result of abnormal expression of CD10 there may be derangements in the CD10-dependent cell growth and apoptosis regulatory signal transduction pathways which lead to uncontrolled cell proliferation and tumorigenesis. Another possible mechanism is that the increased IHC CD10 expression with increasing grade and stage may indicate accumulation of mutated, non-functional CD10 rather than its normal counterpart.[8,31]

Conclusion

The present study revealed that occurrence of urothelial carcinoma was more common in elderly people. Most of the lesions were seen in the age group of 61-70 years. Further it was more common in males than females (9:1).

Most common lesion in the study was low-grade urothelial carcinoma (60%) followed by high-grade urothelial carcinoma (40%). Most of the tumours were seen in the stage pT_1. In our study, out of the total 30 cases of urothelial carcinoma 70% (21/30) were positive for (+1 & +2) CD10 immunostaining.

In our study, a positive rate of CD10 immunoreactivity was detected in 55.6 % (10/18) of low grade papillary urothelial carcinoma and 91.7% (11/12) of high grade papillary urothelial carcinoma which suggest that rate of CD10 positivity increased significantly in higher histological grade of tumor (p-value 0.049).

The positive rate of CD10 expression in our study was 40.0% (4/10) in stage pT_a, 91.7% (11/12) in stage pT_1 and 75.0% (6/8) in stage pT_{2-4} suggesting that CD10 positivity increased significantly in higher pathological stage of tumor as compared to pT_a (p-value 0.009). Degree of expression of CD10 immunostaining score (scale 0-2) was also increased significantly with the higher pathological grade of tumor (p-value 0.009). However we were unable to establish statistically significant correlation between degree of expression of CD10 immunostaining score and pathological stage (p-value 0.210). CD10 immunohistochemical expression in urothelial carcinoma of the urinary bladder showed significant correlation with higher tumor grade and stage and consequently may be associated with tumor invasion and metastasis in bladder cancer pathogenesis. CD10 expression may be used in prognosis prediction of bladder cancer. Most significant limitation of our study is the small number of cases studied. Further studies with larger number of cases may help to clarify small differences between CD10 staining profiles of individual diagnostic entities.

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