Scientific Research

The Role of CK20, p53 and p63 in Differentiation of Some Urothelial Lesions of Urinary Bladder, Immunohistochemical Study

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Abstract

Background: Differentiation of urothelial hyperplasia, dysplasia and carcinoma *in situ* (CIS) may pose diagnostic difficulties. We aim to evaluate the role of CK20, p53 and p63 in differentiation of such lesions. Methods: we evaluate these markers in 213 cases of bladder lesions (14 hyperplasia, 7 dysplasia, 5 CIS, 25 noninvasive and 162 invasive urothelial carcinoma) in a retrospective study on sections from formalin-fixed, paraffin-embedded blocks. Cytoplasmic staining considered for CK20 and nuclear staining for p53 and p63. Results: CK20 was expressed in 14 out of 14 hyperplasia (4 strong, 7 moderate, 3 weak), in 7 out of 7 dysplasia (4 strong , 3 moderate), in 5 out of 5 CIS, in 19 out of 25 noninvasive carcinoma; strong in 11 (7 low grade, 4 high grade), moderate in 7 (5 low grade, 2 high grade), and weak in 1 case of low grade, in 136 out of 162 invasive carcinoma; strong in 46 (22 grade II, 24 grade III), moderate in 71 (2 grade I, 58 grade II, 11 grade III), and weak in 19 (2 grade I, 15 grade II, 2 grade III), no expression in 2 cases of grade IV. p53 was expressed in 7 out of 14 hyperplasia (weak in all cases), in 7 out of 7 dysplasia (5 strong, 2 moderate), in 5 out of 5 CIS (strong in all cases), in 20 out of 25 noninvasive carcinoma (8 strong, 9 moderate, 3 weak), in 135 out of 162 invasive carcinoma (34 strong, 73 moderate, 28 weak). p63 was expressed in 14 out of 14 hyperplasia, in 7 out of 7 dysplasia, in 4 out of 5 CIS, in 25 out of 25 noninvasive carcinoma, and in 134 out of 162 invasive carcinoma (28 strong, 63 moderate, 43 weak). CK20 was insignificant in noninvasive and significant in invasive carcinoma, while p53 and p63 were significant in noninvasive and invasive carcinoma. Conclusion: CK20, p53 and p63 are useful in differentiation of different bladder lesions.

1. Introduction

Urothelial carcinoma is the 7th most common cancer worldwide [1]. More than 50% of patients with non-invasive urothelial tumors have recurrences (or new occurrences), and 10% to 15% of these will progress to invasive cancer [2]. The most important predictive parameter for the biological behavior of urothelial carcinoma, except depth of invasion, is the histological grade of tumor [3], although tumor grade and stage have been shown to have a strong correlation with tumor recurrence and progression to invasive bladder cancer [4]. A large number of markers have been extensively investigated as potential predictors of bladder tumor recurrence, progression, or response to therapy [2]. CK20 belongs to the epithelial subgroup of cytoskeleton-associated intermediate filaments. It has been suggested that CK20 may be an important tool for detecting and identifying these types of cancer (urothelial carcinoma) and may be used as a potential predictors of bladder tumor recurrence, progression, or response to therapy [5]. Mutated p53 gene is a common genetic abnormality in urothelial carcinoma of the bladder. Some studies have depicted that over expression of p53 occurs in higher stages and grades of urothelial carcinoma and over expression of the p53 gene product has been reported as a marker of progression in urothelial carcinoma [6]. p63, a member of the p53 gene family, encodes multiple proteins that may either transactivate p53 responsive genes or act as a dominant-negative factor toward p53. p63 is regulated in bladder carcinogenesis and p63 expression is lost in most invasive cancers whereas non invasive tumors maintain p63 expression [7]. CK20, p53 and p63 immunohistochemistry is suggested to be helpful to distinguish dysplastic changes and carcinoma *in situ* from reactive atypia [8] [9].

2. Material and Methods

This work included 213 cases of different bladder lesions collected from Al-Azhar Faculty of Medicine Hospital labs during the period from January 2005 to January 2010; 43 radical cystectomies and 170 cystoscopic biopsies, 8 cases of normal urothelium included as a control. Four micron thick sections were cut from paraffin blocks of all cases and stained with haematoxylin and eosin (H & E). All cases were re-evaluated; graded and staged according to WHO classification 2004 of bladder tumors and TNM staging 2009 respectively. For immunohistochemistry, sections were taken on poly-L-lysine coated slides. The primary antibodies were as follows: CK20 (Monoclonal mouse anti human cytokeratin 20, Dako cooperation Denmark; colonic carcinoma as positive control & tumor stroma as negative control), p53 (Monoclonal mouse anti human p53, Lab Vision Cooperation Fremount USA; Breast cancer as positive control & normal liver tissue as negative control), p63 (Monoclonal mouse anti human p63, Biocare Medical Cooperation Concord USA; normal prostate as positive control & muscle tissue as negative control). Cytoplasmic staining was considered for CK20 and nuclear staining for p53 and p63. According to Yildiz's *et al.*, (2009) [10], CK20 cytoplasmic staining was evaluated: (0; no staining), (1+; patchy or/and weak), (2+; <50% cells, moderate), (3+; >50% cells, strong). p53 was evaluated according to number of positive cells (0; no staining), (1+; <15% cells, weak), (2+; 15% - 50% cells, moderate), (3+; >50% cells, strong). According to Kaufmann's *et al.* (2001) [11], p63 was evaluated according to the percentage of positive cells, (1+; 1% - 10%), (2+; 11% - 50%), and (3+; more than 50%).

3. Statistical Analysis

Statistical presentation and analysis of the present study was conducted, using the mean, standard error, student t-test and Chi-square by SPSS V17.Statistical significance was established as $P < 0.05$ [12] [13].

4. Results

This study consisted of 213 cases of bladder lesions and 8 cases of normal urothelium as a control. The age of the patients ranged from 29 to 84 years (mean: 59.4) with 204 males and 9 females.

Histopathological findings:

Urothelial hyperplasia (14 cases): of flat and papillary types, and associating different types of cystitis (6 bilharzial, 5 polypoid, 1 interstitial, 1 lymphoid and 1 hemorrhagic) (see **Figure 1**).

Urothelial dysplasia (7 cases): with variable loss of polarity, irregular nuclear borders, inconspicuous nucleoli and rare mitoses, moderate in 5 cases and severe in 2 cases.

Urothelial CIS (5 cases): associating invasive carcinoma, showing high grade nuclear anaplasia, large pleomorphic nuclei, frequent mitoses, and involving the entire epithelial thickness (see **Figure 2**).

Urothelial carcinoma (187 cases): According to WHO classification (2004), 25 cases of non invasive papillary carcinoma (18 low grade and 7 high grade) and according to TNM staging (2009), all cases staged as pTa, and 162 cases of invasive urothelial carcinoma (8 grade I, 111 grade II, 41 grade III and 2 grade IV), and staged as (69 pT1, 62 pT2, 26 pT3, 5 pT4) (see **Table 1** & **Figure 3**).
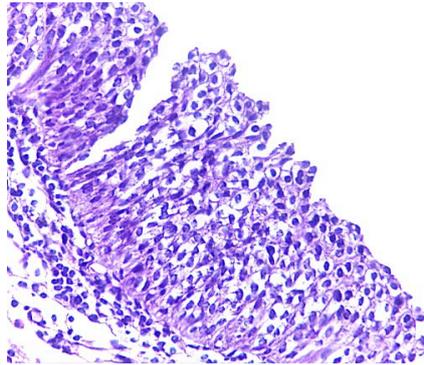
Figure 1. Urothelial hyperplasia showing benign-looking hyperplastic urothelium (H & E × 200).
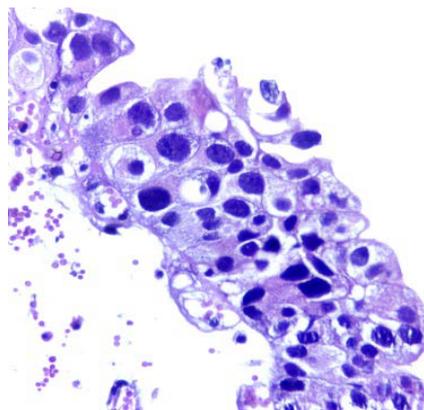
Figure 2. Urothelial CIS showing replacement of urothelium by malignant cells with nuclear anaplasia, with no invasion (H & E × 400).
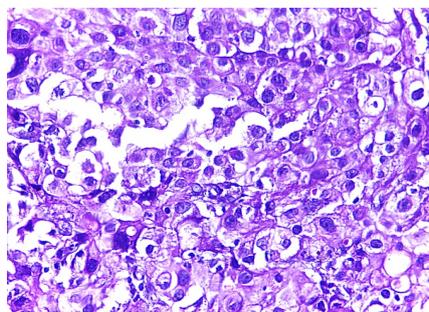
Figure 3. Invasive urothelial carcinoma grade III showing groups of malignant urothelial cells with marked anaplasia (H & E × 360).

Table 1. Grading and staging of the studied invasive urothelial carcinomas.

Stage		Grade (Invasive Carcinoma)				
		Grade I	Grade II	Grade III	Grade IV	Total
pT1	N	8	59	2	0	69
	%	4.94	36.42	1.23	0.00	42.59
pT2	N	0	44	16	2	62
	%	0.00	27.16	9.88	1.23	38.27
pT3	N	0	8	18	0	26
	%	0.00	4.94	11.11	0.00	16.05
pT4	N	0	0	5	0	5
	%	0.00	0.00	3.09	0.00	3.09
Total	N	8	111	41	2	162
	%	4.94	68.52	25.31	1.23	100.00
Chi-square	X^2			75.838		
	P-value			0.000		

Immunohistochemical findings:

CK20

Normal urothelium (8 cases): CK20 was expressed in all cases and localized to the superficial umbrella cell layer (strong in 1, moderate in 5 and weak in 2).

Urothelial Hyperplasia (14 cases): CK20 was expressed in all cases and limited to the superficial umbrella cell layer (strong in 4, moderate in 7 and weak in 3).

Urothelial Dysplasia (7 cases): CK20 was expressed in all cases, in upper 2/3 of urothelium in 6 cases (strong in 4 and moderate in 2), and moderate throughout the uroithelium in 1case, (see **Figure 4**). Urothelial CIS (5 cases): CK20 was strongly expressed throughout the urothelium in all cases.

Non-invasive papillary carcinoma (25 cases): CK20 was expressed in 19 cases (76%), strong in 11 (44%), moderate in 7 (28%) and weak in 1 (4%), (see **Table 2** & **Figure 5**).

Invasive urothelial carcinoma (162 cases): CK20 was expressed in 136 cases (84%), strong in 46 (28.4%), moderate in 71 (43.9%) and weak in 19 (11.7%), (see **Table 3**, **Table 4** and **Figure 6**).

p53

Normal urothelium (8 cases): p53 was expressed in 3 cases (37.5%; seen in basal and intermediate layers) while the other 5 cases showed no reactivity.

Urothelial hyperplasia (14 cases): p53 was expressed in 7 (50%; seen in basal and intermediate layers) while the other 7 cases showed no reactivity.

Urothelial Dysplasia (7 cases): p53 was expressed throughout the urothelium in all cases (strong in 5 and moderate in 2).

Urothelial CIS (5 cases): p53 was expressed throughout the urothelium in all cases, (see **Figure 7**).

Non-invasive papillary carcinoma (25 cases): p53 was expressed in 20 cases (80%), strong in 8 (32%), moderate in 9 (36%) and weak in 3 (12%), (see **Table 5** & **Figure 8**).
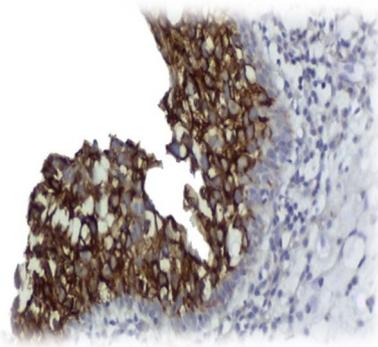
Invasive urothelial carcinoma (162 cases): p53 was expressed in 135 cases (83.33%), strong in 34 (20.99%), moderate in 73 (45.06%) and weak in 28 (17.28%), (see **Table 6** & **Table 7**).

p63

Normal urothelium (8 cases): p63 was strongly expressed in basal and intermediate layers of all cases while the superficial umbrella cells showed no reactivity.

Urothelial Hyperplasia (14 cases): p63 was strongly expressed in basal and intermediate layers of all cases while the superficial umbrella cells showed no reactivity.

Urothelial Dysplasia (7 cases): p63 was expressed in all cases; strong in basal layers with gradual decrease towards the epithelial surface.

Figure 4. Urothelial dysplasia strongly positive for CK20, and positivity was seen in upper 2\3 of urothelium(DAB × 235)
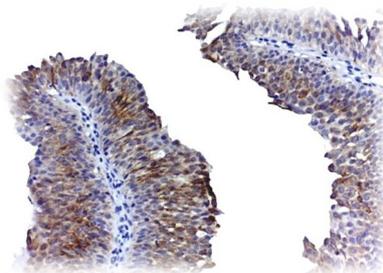
Figure 5. Low-grade non-invasive papillary urothelial carcinoma moderately positive for CK20 (DAB × 200).
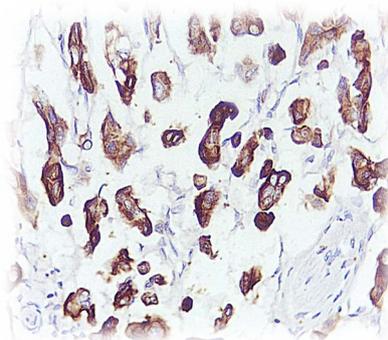
Figure 6. Invasive urothelial carcinoma grade III strongly positive for CK20 (DAB × 400).
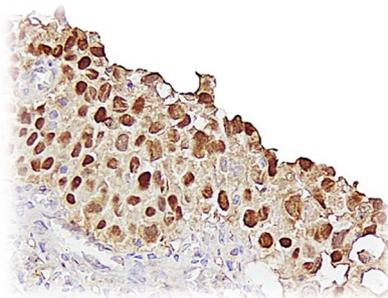
Figure 7. Urothelial CIS strongly positive for p53 and positivity was seen throughout urothelial thickness (DAB × 235).

Figure 8. High grade non-invasive papillary urothelial carcinoma strongly positive for P53 (DAB × 235).

Table 2. Correlation of CK20 immunoreactivity to tumor grade of non-invasive papillary urothelial carcinoma.

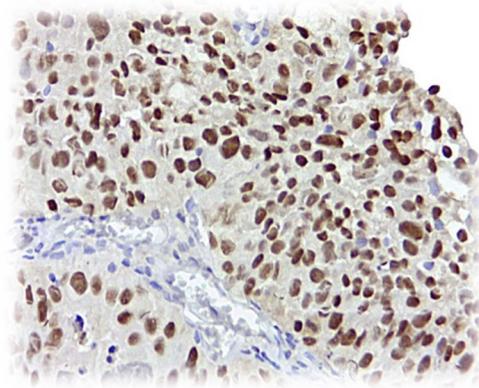| Tumor grade		CK20				
		Negative	Weak	Moderate	Strong	Total
Low grade	N	5	1	5	7	18
	%	28	6	28	39	100
High grade	N	1	0	2	4	7
	%	14	0	29	57	100
Total	N	6	1	7	11	25
	%	24	4	28	44	100
Chi-square	X^2			1.445		
	P-value			0.695		

Statistically insignificant (P-value: 0.695). So, CK20 expression is different in low and high grades of non-invasive papillary urothelial carcinoma.

Table 3. Correlation of CK20 immunoreactivity to tumor grade of invasive urothelial carcinoma.

Grade		CK20				
		Negative	Weak	Moderate	Strong	Total
Grade I	N	4	2	2	0	8
	%	50.00	25.00	25.00	0.00	100.00
Grade II	N	16	15	58	22	111
	%	14.41	13.51	52.25	19.82	100.00
Grade III	N	4	2	11	24	41
	%	9.76	4.88	26.83	58.54	100.00
Grade IV	N	2	0	0	0	2
	%	100.00	0.00	0.00	0.00	100.00
Total	N	26	19	71	46	162
	%	16.05	11.73	43.83	28.40	100.00
Chi-square	X^2			39.017		
	P-value			<0.001[*]		

Statistically significantly (P value: <0.001). So, CK20 expression had a direct correlation with grade of invasive urothelial carcinoma.

Table 4. Correlation of CK20 immunoreactivity to tumor stage of invasive urothelial carcinoma.

Tumor stage		CK20				
		Negative	Weak	Moderate	Strong	Total
Stage Ta	N	6	1	7	11	25
	%	24.00	4.00	28.00	44.00	100.00
Stage T1	N	13	11	39	6	69
	%	18.84	15.94	56.52	8.70	100.00
Stage T2	N	9	7	25	21	62
	%	14.52	11.29	40.32	33.87	100.00
Stage T3	N	4	1	7	14	26
	%	15.38	3.85	26.92	53.85	100.00
stage T4	N	0	0	0	5	5
	%	0.00	0.00	0.00	100.00	100.00
Total	N	32	20	78	57	187
	%	17.11	10.70	41.71	30.48	100.00
Chi-square	X^2			43.840		
	P-value			0.000		

Statistically significant (P value: 0.000). So, CK20 expression had a direct correlation with stage of invasive urothelial carcinoma.

Table 5. Correlation of p53 immunoreactivity to tumor grade of non-invasive papillary urothelial carcinoma.

Grade		p53				
		Negative	Weak	Moderate	Strong	Total
Low grade	N	5	3	7	3	18
	%	27.78	16.67	38.89	16.67	100.00
High grade	N	0	0	2	5	7
	%	0.00	0.00	28.57	71.43	100.00
Total	N	5	3	9	8	25
	%	20.00	12.00	36.00	32.00	100.00
Chi-square	X^2			7.983		
	P-value			0.046		

Statistically significant (P-value: 0.046). So, p53 expression had a direct correlation with the grade of non-invasive urothelial carcinomas.

Table 6. Correlation of p53 immunoreactivity to tumor grade of invasive urothelial carcinoma.

Grade		p53				
		Negative	Weak	Moderate	Strong	Total
Grade I	N	2	4	2	0	8
	%	25.00	50.00	25.00	0.00	100.00
Grade II	N	18	20	59	14	111
	%	16.22	18.02	53.15	12.61	100.00
Grade III	N	5	4	12	20	41
	%	12.20	9.76	29.27	48.78	100.00
Grade IV	N	2	0	0	0	2
	%	100.00	0.00	0.00	0.00	100.00
Total	N	27	28	73	34	162
	%	16.67	17.28	45.06	20.99	100.00
Chi-square	X^2			36.516		
	P-value			0.000		

Statistically significant (P value: 0.000). So, p53 expression had a direct correlation with grade of invasive urothelial carcinoma.

Urothelial CIS (5 cases): p63 was strongly expressed throughout of the urothelium in 4 cases, and in basal layers with gradual decrease towards the epithelial surface in 1case.

Non-invasive papillary carcinoma (25 cases): p63 was expressed in all cases and ranged from moderate to strong, see (**Table 8**).

Invasive urothelial carcinoma (162 cases): p63 was expressed in 134 cases (82.71%), strong in 28 (17.28 %), moderate in 63 (38.89%) and weak in 43 (26.54 %), see (**Table 9** & **Table 10**) and (**Figure 9**).

Table 7. Correlation of p53 immunoreactivity to tumor stage of invasive urothelial carcinoma.

Stage		p53				
		Negative	Weak	Moderate	Strong	Total
pTa	No.	5	3	9	8	25
	%	20.00	12.00	36.00	32.00	100.00
pT1	No.	14	13	37	5	69
	%	20.29	18.84	53.62	7.25	100.00
pT2	No.	12	14	28	8	62
	%	19.35	22.58	45.16	12.90	100.00
pT3	No.	1	1	8	16	26
	%	3.85	3.85	30.77	61.54	100.00
pT4	No.	0	0	0	5	5
	%	0.00	0.00	0.00	100.00	100.00
Total	No.	32	31	82	42	187
	%	17.11	16.58	43.85	22.46	100.00
Chi-square	X^2			53.364		
	P-value			0.000		

Statistically significant (P value: 0.000). So, p53 expression had a direct correlation with stage of urothelial carcinoma.

Table 8. Percentage of positive p63 cells in correlation with the grade of non-invasive papillary urothelial carcinoma.

% of cells				T-test	
Grade (non-invasive carcinoma)	No.	Mean	SD	t	P-value
Low grade	18	90.278	5.809	7.481	<0.001[*]
High grade	7	65.000	11.180		

Statistically significant (P-value: <0. 001). So, p63 expression had an inverse correlation with grade of non invasive urothelial carcinomas.

**Table 9.** Correlation of p63 immunoreactivity to tumor grade of invasive urothelial carcinoma.

Grade		p63				
		Negative	Weak	Moderate	Strong	Total
Grade I	N	0	0	1	7	8
	%	0.00	0.00	12.50	87.50	100.00
Grade II	N	9	26	55	21	111
	%	8.11	23.42	49.55	18.92	100.00
Grade III	N	17	17	7	0	41
	%	41.46	41.46	17.07	0.00	100.00
Grade IV	N	2	0	0	0	2
	%	100.00	0.00	0.00	0.00	100.00
Total	N	28	43	63	28	162
	%	17.28	26.54	38.89	17.28	100.00
Chi-square	X^2			71.168		
	P-value			0.000		

Statistically significant (P value: 0.000). So, p63 expression had an inverse correlation with grade of invasive urothelial carcinomas.

Table 10. Correlation of p63 immunoreactivity to tumor stage of invasive urothelial carcinoma.

Stage		p63				
		Negative	Weak	Moderate	Strong	Total
pTa	N	0	0	1	24	25
	%	0.00	0.00	4.00	96.00	100.00
pT1	N	3	11	30	25	69
	%	4.35	15.94	43.48	36.23	100.00
pT2	N	13	18	28	3	62
	%	20.97	29.03	45.16	4.84	100.00
pT3	N	7	14	5	0	26
	%	26.92	53.85	19.23	0.00	100.00
pT4	N	5	0	0	0	5
	%	100.00	0.00	0.00	0.00	100.00
Total	N	28	43	64	52	187
	%	14.97	22.99	34.22	27.81	100.00
Chi-square	X^2			134.741		
	P-value			0.000		

Statistically significant (P value: 0.000). So, p63 expression had an inverse correlation with stage of invasive urothelial carcinomas.
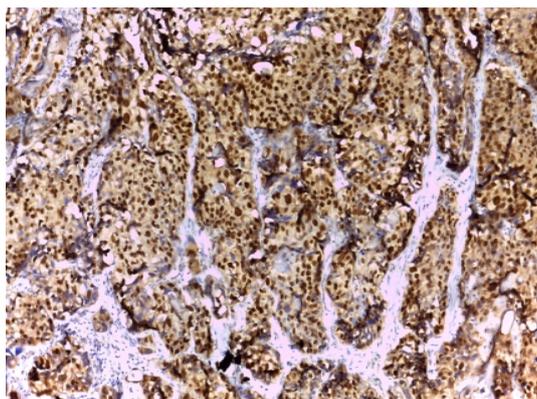
Figure 9. Invasive urothelial carcinoma grade II strongly positive for p63 (DAB ×150).

5. Discussion

The aim of this work is to evaluate the role of CK20, p53 and p63 in differentiation between urothelial hyperplasia, dysplasia, and grade and stage of the urothelial carcinoma.

In the current study, CK20 was expressed in all cases of normal urothelium and the expression was limited to the superficial umbrella cell layer and the reaction was moderate in most of cases, similar findings were reported by Southgate *et al.*, (1999) [14] who noted that normal urothelium showed CK20 cytoplasmic immunoreactivity in the superficial umbrella cell layer and this was named the normal CK20 expression pattern. Castillo-Martin *et al.*, (2010) [15] studied molecular pathways of urothelial development and bladder tumorigenesis and found that umbrella cells are characterized by expression of CK18 and CK20.

In this work, scattered CK20 immunoreactivity was demonstrated in all cases of dysplasia and the reaction was documented in the upper two thirds of the urothelial thickness in 85.7% of cases, it involved the whole thickness of the urothelium in 14.3%. these findings are parallel to those of Harnden *et al.*, (1996) [16] who found that the expression of CK20 was restricted to superficial "umbrella" cells, even in the presence of severe

inflammation while in the vast majority of cases of dysplasia, it was seen at least focally with positive expression in all layers of the urothelium.

In this work, all cases of CIS showed strong CK20 positivity in the majority of malignant cells and the positivity was through the full thickness of the urothelium. Similar findings were reported by Mallofré *et al.*, 2003 [8], (McKenney *et al.*, 2001, Yin *et al.*, 2006 & Nese *et al.*, 2009) [17]-[19] who found intense CK20 positivity in the vast majority of cases of urothelial CIS in the majority of malignant cells through the full thickness of the urothelium.

In the current study, CK20 was expressed in 82.89% of the cases of urothelial carcinoma and the reaction was strong in 30.48%, moderate in 41.71% and weak in 10.7% of cases. Similar findings were reported by Moll *et al.*, 1992, Miettinen *et al.*, 1995 and Wang *et al.*, 1995) [20]-[22] who found the expression of CK20 in different human cancers and found that the majority of cases of urothelial carcinoma showed positive CK20 expression.

In this work, p53 was not expressed in non-neoplastic urothelium (including normal and hyperplastic urothelium) apart from occasional weak positivity in the basal and intermediate layers in some cases, these findings are parallel to those of Mallofré *et al.*, 2003 [8], Yildiz *et al.*, 2009) [10], (McKenney *et al.*, 2001 [17] & Kalantari and Ahmadnia, 2007 [23] who found that p53 immunoreactivity in normal urothelium ranged from negative to weak and patchy and in reactive urothelium, p53 expression was predominantly negative with occasional weak positivity in the basal and intermediate cells. These results support the view that the absence of p53 in urothelium points to its non neoplastic nature. However, Soukup *et al.*, (2007) [24] found p53 positivity in some cases of non-tumor mucosa of urinary bladder in patients with superficial bladder cancer. These cases with p53 positivity in non-tumor mucosa showed higher recurrence rate than that with normal p53 negative non-tumor mucosa.

In this study, p53 positivity of moderate to strong intensity was documented in all the studied cases of dysplasia and the expression was scattered throughout the urothelium. Similar finding was reported by Yildiz *et al.*, (2009) [10] who found that most of the cases of dysplasia had p53 positivity in scattered cells through the urothelium.

Many workers Mallofré *et al.*, 2003 [8], Yildiz *et al.*, 2009) [10], (McKenney *et al.*, 2001 [17] & Nese *et al.*, 2009 [19] demonstrated strong p53 positivity in the majority of cases of urothelial CIS in most of malignant cells throughout the urothelium, an expression similar to that found in the current study. Contrary to these findings are those of Nakopoulou *et al.*, (1998) [25] who did not demonstrate p53 expression in the dysplastic urothelia examined.

In the current study, p53 was expressed in 82.89% of the cases of urothelial carcinoma and the reaction was strong in 22.46%, moderate in 43.85% and weak in 16.58% of cases. Similar findings were reported by (Thomas *et al.*, 1994, Burkhard *et al.*, 1997, Grossman *et al.*, 1998, Uchida *et al.*, 2002, Babjuk *et al.*, 2003 & Venyo *et al.*, 2010) [26]-[31] who found p53 expression in the majority of cases of urothelial carcinoma.

In the current study, in all cases of dysplasia and 1case of CIS, p63 expression showed a maximum intense reaction in the nuclei of basal epithelial cells, which was gradually diminished towards the epithelial surface. Most (80%) of the cases of CIS showed strong positivity for p63 in all layers of the urothelium.

Many studies Di Como *et al.*, 2002 [7], Kaufmann *et al.*, 2001 [11], (Yang *et al.*, 1998, Koga *et al.*, 2003, Karni-Schmidt *et al.*, 2011 & Pignon *et al.*, 2013) [32]-[35] demonstrated that non-neoplastic urothelium (including normal and reactive hyperplastic urothelium) showed strong positive nuclear immunoreactivity to p63 in entire basal and parabasal cells but immunoreactivity was undetectable in umbrella cells, an expression similar to that found in all studied cases of the non-neoplastic urothelium in the current study.

In the current study, p63 was expressed in 85.02% of the cases of urothelial carcinoma and the reaction was strong in 27.81%, moderate in 34.22% and weak in 22.99% of cases. This agrees with the results of Kaufmann *et al.*, (2001) [11] who found that the majority of cases (more than 70%) of urothelial carcinoma were p63 positive. This agrees also with the results of Di Como *et al.*, (2002) [7] who studied the expression of p63 in some different human normal and tumor tissues and showed that p63 is expressed in most of the cases of urothelial carcinoma.

In the current study, p63 was expressed in all cases of non-invasive papillary urothelial carcinoma and the reaction ranged from moderate to strong in most of the cells. Similar findings were reported by Urist *et al.*, (2002) [36] who found that low-grade papillary superficial bladder tumors expressed p63 in 93% of tumor cells. However in the high-grade superficial tumors, there was a significant reduction in p63 positivity to 68%.

In the current study, p63 was expressed in 83.33% of the cases of invasive urothelial carcinoma and the reac-

tion was strong in 20.99%, moderate in 45.06% and weak in 17.28% of cases, these findings are in agreement with Chuang *et al.*, (2007) & Srinivasan and Parwani (2011) [37]-[38] who showed that urothelial carcinomas usually show p63 positivity while prostate carcinomas always show p63 negativity. Thus p63 expression can be used as a useful tool in distinguishing urothelial carcinomas from prostate carcinoma.

6. Conclusion

We conclude that there is a role of CK20, p53 and p63 in differentiating non-neoplastic lesions, dysplastic lesions and urothelial carcinoma, and these markers can be used as potential predictors of biologic behavior of urothelial carcinoma. We recommended performing many prospective studies with clinical correlation between these markers and the progression of urothelial tumors with large series of patients.

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