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CORRELATION OF GATA3 EXPRESSION WITH HISTOPATHOLOGICAL PARAMETERS IN PATIENTS WITH UROTHELIAL CARCINOMA

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ABSTRACT

Introduction: Urothelial carcinoma is one of the most common genitourinary system malignancies. Most of these tumours are low-grade and easily recognised histopathologically, but a significant number of high-grade cases should be diagnosed and differentiated from metastasis or direct extension, especially from prostate and kidney cancers, as they differ in treatment and prognosis. GATA3 is one of the recently used immunohistochemical markers for urothelial carcinoma differentiation, and its intensity significantly correlates with tumour grade and stage, decreasing with higher stage and grade. The aim of study is to GATA3 value in distinguishing urothelial carcinoma, prostatic adenocarcinoma, and renal cell carcinoma of papillary and clear cell types and GATA3 expression correlates with clinicopathological markers such grade, stage, necrosis, and mitosis. **Method:** 70 paraffin-embedded blocks of urothelial carcinoma, 10 of prostatic adenocarcinoma, and 10 of renal cell carcinoma of papillary and clear cell variants were selected between January 2017 and September 2020. They were stained with haematoxyline and eosin, histopathologically evaluated, then stained with GATA3 antibody and reevaluated with semi quantitative immunoreactive score. GATA3 correlated with tumour grade, stage, necrosis, and mitosis. **Results:** GATA3 was expressed in 84.3% of urothelial carcinoma patients and was substantially linked with tumour grade ($p = 0.001$) and stage ($p = 0.003$), but not mitosis or necrosis. **Conclusion:** GATA3 can detect urothelial origin. If utilised in clinical contexts, it is successful. GATA3 expression predicts cancer recurrence independently, making it a prognostic marker as well. In this study, GATA3 expression did not affect necrosis or mitosis.

KEYWORDS: GATA3, expression, histopathological parameters, urothelial carcinoma.

INTRODUCTION

Bladder cancer is the 10th most frequent disease globally and causes 2.1% of cancer deaths.[1] The male-to-female ratio is 3.5:1.[2] According to the International Agency for Research on Cancer, it is the 5th most prevalent cancer in males (7.4%) and the 4th most common in females (4.6%) in Iraq, and it causes 3.5% of cancer deaths yearly. Its prevalence increases largely in developing nations.[1] Smoking causes 65% of male and 30% of female bladder cancer in industrialised nations.[3] Aniline dyes—especially benzidine and β naphthylamine—auramines, phenacetin, and cyclophosphamide—are also environmental influences. Schistosoma haematobium causes bladder urothelial and squamous cell cancer. Most research demonstrates that HPV does not cause this malignancy. Radiation treatment for prostatic cancer may raise the incidence of bladder carcinoma.[4] In wealthy nations, 65% of bladder cancer patients survive at least 5 years following diagnosis, however this varies by stage.[3] 90% of bladder initial tumours are urothelial carcinoma (TCC). Like other carcinomas, it develops from hereditary and environmental causes. Chemical variables are considered crucial.[4] Urothelial carcinoma of the bladder is rare in children and young adults but common in those over 50. In young adults, low-grade, indolent neoplasms can be aggressive.[4] Men are impacted more than women, and white people more than African-Americans.[4] Ethnicity does not seem to matter.[5] Gross or microscopic hematuria is most prevalent, followed by subsequent urinary tract infection symptoms. High-grade tumours typically produce dysuria due to bladder wall involvement. Bladder urothelial tumours can occur anywhere. In nearly 1000 cases, the lateral walls were

the most frequent and the anterior wall the least common, 4%. Also seen in bladder diverticula. They can cause hydronephrosis and pyelonephritis by blocking one or both ureters surrounding the orifices. Metachronous multicentricity is prevalent.[4] Most urothelial malignancies (UC) are superficial at diagnosis, and 70% have a lengthy clinical history with numerous recurrences after local excision without tumour development. A lesser but considerable minority of individuals arrive with aggressive malignancies that progress quickly. Thus, urinary bladder cancer is a costly illness that requires lifetime surveillance.[2] GATA3, a transacting T-cell-specific transcription factor encoded by the GATA3 gene, is crucial to endothelial cell function.[6] This marker distinguishes urothelium, breast epithelium, and T-lymphocyte subsets. Invasive bladder cancer down-regulates it, helping distinguish urothelial from prostatic adenocarcinoma.[7] This study aims to explore the utility of GATA binding protein 3 expressions in urothelial carcinoma, and in predicting the probable grade and stage in biopsy material with poor morphological characteristics.

METHOD

This study is a retrospective cross section, carried out in Karbalaa holy city, at the laboratories of Al-Hussain Teaching Hospital, Al-Kafeel specialized hospital, and Al-Sajjad private lab., during the period of (jan. 2017 to September 2020).

Inclusion criteria: any patient with genitourinary cancer that have been diagnosed in the period between january 2017 and December 2019. All ages will be included. Males and females will be included. Only nuclear positivity will be included.

Exclusion criteria: All specimens without or with inadequate muscularis propria will be discarded, cases of renal cell carcinoma other than clear cell or papillary variants. Seventy cases with urothelial carcinoma, ten cases of prostatic adenocarcinoma, and ten cases of renal cell carcinoma of papillary and clear cell variants were selected, all the cases were formalin fixed, then paraffin embedded. The type of biopsy for urothelial carcinoma was TURT and radical cystectomy, prostatic adenocarcinoma type of biopsy true-cut biopsy and TURP, and for RCC core biopsy and partial or radical nephrectomy. All cases were histopathologically reevaluated by a histopathology consultant to confirm the diagnosis, grade, presence or absence of muscle invasion, presence or absence of necrosis, and number of mitosis. These cases were collected from Al-Hussain teaching hospital, Al-Kafeel specialized hospital, and Al-Sajjad private lab. Control group; ten cases of well differentiated breast carcinoma, normal salivary gland tissue also collected from the histopathology lab in AL-Hussain Teaching Hospital in Karbala, as well as Al-kafeel specialized hospital, and Al-Sajjad private lab in the same period proved by the microscopical examination were considered as positive control group. Negative control group were sections untreated with primary antibody (GATA3). The used scoring system is the semi quantitative immunoreactive score (IRS), which gives a range of 0–12 as a product of multiplication between positive cells proportion score (0–4) and staining intensity score (0–3) table3, If the examined sample stains for IHC marker is with heterogeneity, then each intensity of staining is scored independently and the results are summed. For example, when a specimen contained 50% of the tumor cells with moderate intensity (2 × 2 = 4), 25% of tumor cells with intense immunostaining (1 × 3 = 3), and 25% of cells with weak intensity (1 × 1 = 1), the score was 4 + 3 + 1 = 8.[8,9] Statistical Analysis of all results were performed by the help of SPSS statistical package at level of significance alpha=0.05 to find (P value).

RESULTS

Seventy cases of urothelial carcinoma, ten cases of prostatic adenocarcinoma, and ten cases of renal cell carcinoma were included in this study. With an age range for urothelial carcinoma from 34 to 88 years, mean 73.5, including 53males (75.7%) and 17 females (24.3%), with male to females ratio3.11:1, non- invasive urothelial carcinoma (Ta and T1) account for 36 (51.4%) of the cases, and invasive urothelial carcinoma (T2, T3, and T4) cases account for 34 (48.6%). 35 (50%) of the cases were low grade and 35 (50%) were high grade. Age range for prostatic adenocarcinoma was (52 to 85) with mean 68.1, according to gleason's grading system 1 case (10%) grade 1,1 case (10%) grade 2, 1 case (10%) grade 3, 5 cases (50%) grade 4, and 2 cases (20%) grade 5. And the age range for renal cell carcinoma was (28 to 70) years with mean 52.2, four of the cases were females (40%), and six of them were males (60%), with male to female ratio 1.5:1, according to WHO / International Society of Urologic Pathology (ISUP) Grading for Clear Cell and Papillary RCC, two of the cases (20%) were grade 1, five of them (50%) were grade 2, and three of the selected cases (30%) were grade 3. As show in table 1.

Table 1: Distribution of urothelial carcinoma and Adenocarcinoma and Renal cell carcinoma according to clinicopathological parameters.

Clinicopathological parameters		Urothelial carcinoma cases	
		number	percentage
age	65 years or less	39	55.7%
	More than 65 years	31	44.3%
gender	male	53	75.7%
	female	17	24.3%
stage	Ta	13	18.6%
	T1	23	32.9%
	T2	27	38.6%
	T3	2	2.9%
	T4	5	7.1%
Grade	Low grade	35	50%
	High grade	35	50%
mitosis	Less than 5/10HPF	38	54.3%
	5_10/10HPF	23	32.9%
	More than 10/10HPF	9	12.9%
necrosis	absent	56	80%
	present	14	20%

Clinicopathological parameters		Adenocarcinoma cases	
		number	percentage
age	65 year or less	6	60%
	More than 65 year	4	40%
Gleason grade	Grade 1	1	10%
	Grade 2	1	10%
	Grade 3	1	10%
	Grade 4	5	50%
	Grade 5	2	20%

Clinicopathological parameters		Renal cell carcinoma cases	
		number	percentage
Age	65 years or less	8	80%
	More than 65 years	2	20%
Gender	male	6	60%
	female	4	40%
Grade	Grade 1	2	20%
	Grade 2	5	50%
	Grade 3	3	30%

Immunohistochemical evaluation of GATA3 was determined by nuclear staining of the malignant cells using semiquantitative immunoreactive scoring system IRS[118,119,120], in which the percentage and intensity of staining were included in this system. IRS ranged from zero to twelve, positive cases were recorded when the score is two or more, 59 cases (84.3%) recorded as positive all with diffuse non-focal staining. Cases grouped into four groups where 0_1 score regarded as negative (group 1), 2_4 weakly positive (group 2), 5_8 moderately positive (group 3), and 9_12 strongly positive (group 4). As show in table 2.

Table 2: Immunohistochemical expression of GATA3 in urothelial carcinoma.

group	GATA3 expression	Numberof patients	percentage
group 1	Negative	11	15.7%
Group 2	Weak	21	30%
Group 3	Moderate	19	27.1%
Group 4	strong	19	27.1%

Expression of GATA3 protein in urothelial carcinoma in association with grade revealed that positive GATA3 reported in 33 out of 35 of low grade cases (94.2% of the cases), and 26 out of 35 cases of the high grade tumors (74.2% of the cases). There is significant correlation between GATA3 staining and tumor grade with P value is significant (less than 0.05). As show in table 3.

Table 3: Association of GATA3 reactivity and urothelial carcinoma grade.

Tumor grade	Positive cases		Negative cases		Total		
	No.	%	No.	%	No.	%	
Low	33	94.2%	2	5.7%	35	50%	P value < 0.05
High	26	74.2%	9	25.7%	35	50%	
Total	59	84.3%	11	15.7%	70	100%	

Expression of GATA3 in relation to stage revealed that with increased pathologic T stage, GATA3 staining decrease in intensity and percentage, significantly with stage 3 and 4, with all the 13 Ta cases (100%) were moderately to strongly positive, 22 out of the 23 T1 cases (95.6%) were positive, 20 cases of the 27 T2 cases were positive (74%), one case out of the two T3 cases was positive (50%), and, and 3out of the five T4 cases were positive (60%). This is a significant correlation between GATA3 and tumor stage P value < 0.05. As show in table 4.

Table 4: GATA3 association with urothelial carcinoma stage.

Tumor stage	GATA3 score groups										
	negative		positive								
	Score0_1		Score 2_4		Score 5_8		Score 9_12				
	N	%	N	%	N	%	N	%	total		
Stage Ta	0	0%	0	0%	4	21.1%	9	47.4%	13	18.6%	**P value <0.05 (0.003)**
Stage T1	1	9.1%	9	42.8%	8	42.1%	5	26.3%	23	32.8%	
Stage T2	7	63.6%	10	47.6%	5	26.3%	5	26.3%	27	38.6%	
Stage T3	1	9.1%	1	4.8%	0	0%	0	0%	2	2.9%	
Stage T4	2	18.2%	1	4.8%	2	10.5%	0	0%	5	7.1%	
total	11	15.7%	21	30%	19	27.1%	19	27.1%	70	100%	

Correlation between GATA3 expression and number of mitoses revealed that 35 case (92.1%) of 38 case with mitosis less than 5/10HPF were positive, 17 (73.9%) case out of 23 case with 5_10 mitosis/10HPF were GATA3 positive, and 7 cases (77.7%) out of 9 cases with mitosis >10/10HPF were positive, despite the presence of correlation, but it's not significant P value 0.2. As show in table 5.

Table 5: GATA3 association with number of mitosis.

mitosis	GATA3 expression						
	positive		negative		total		
	number	%	number	%	number	%	
<5/10HPF	35	92.1%	3	7.9%	38	54.4%	P value > o.o5
5_10/10HPF	17	73.9%	6	26.1%%	23	32.8%	
>10/10HPF	7	77.7%	2	22.2%	9	12.8%	
total	59	84.2%	11	15.7%	70	100%	

Regarding correlation between GATA3 reactivity and presence of necrosis, 11 out of 14 cases (78.6%) with necrosis were GATA3 positive, and 48 case out of 56 (85.7%) without necrosis were GATA3 positive. The correlation is not significant P value = 0.07. As show in table 6.

Table 6: correlation with presence or absence of necrosis.

	Positive cases		Negative cases		Total		
	No.	%	No.	%	No.	%	
present	11	78.6%	3	21.4%	14	20%	**>0.05 P value**
absent	48	85.7%	8	14.2%	56	80%	
Total	**59**	**84.3%**	**11**	**15.7%**	**70**	**100%**	

All cases of prostatic adenocarcinoma were GATA3 negative.

Table 7: GATA3 expression in prostatic adenocarcinoma. GATA3 expression in renal cell carcinoma (clear cell and papillary variants).

Tumor	Positive		Negative		Total	
	No.	%	No.	%		P value < 0.05
Urothelial carcinoma	59	83.4%	11	15.7%	70	
Prostatic adenocarcinoma	0	0%	10	100%	10	(0.01)
total	59		21		80	

Tumor	Positive		Negative		Total	
	No.	%	No.	%		P value < 0.05
Urothelial carcinoma	59	83.4%	11	15.7%	70	
RCC	0	0%	10	100%	10	(0.01)
total	59		21		80	

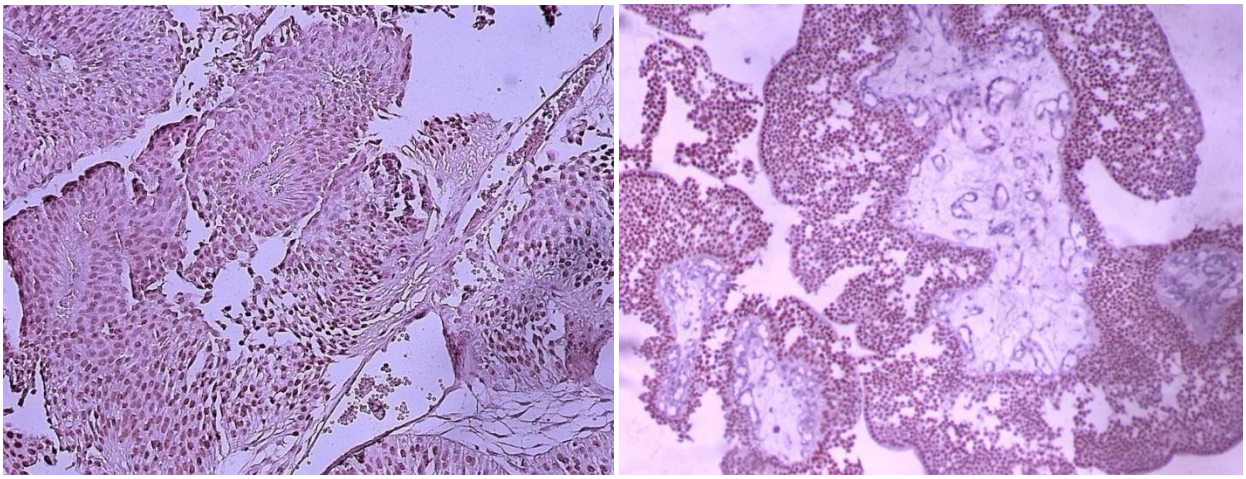

Figure 1: GATA3 expression in Low grade papillary urothelial carcinoma.

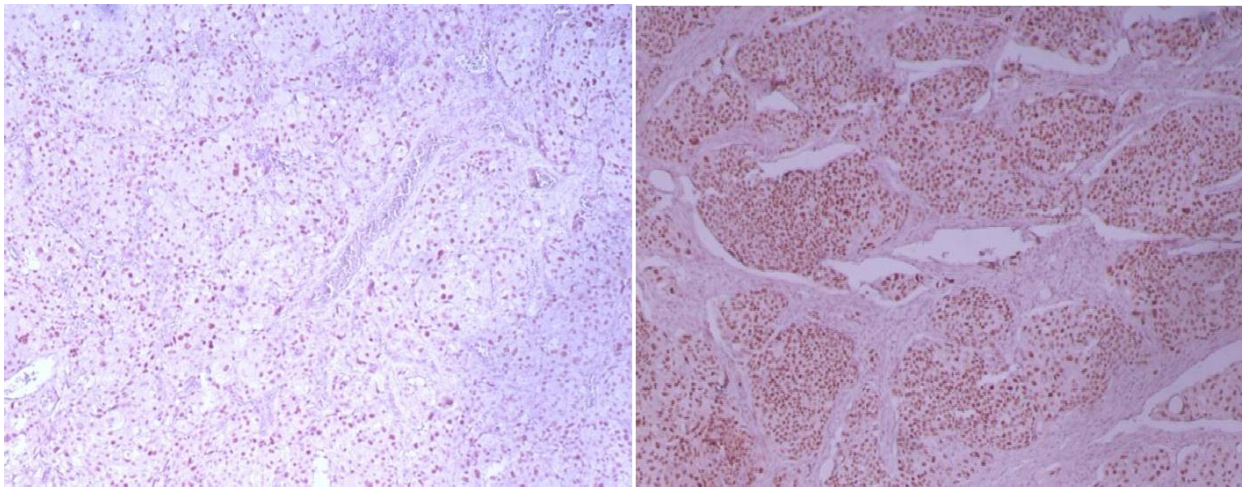

Figure 2: GATA3 expression in high grade urothelial carcinoma.

DISCUSSION

Approximately 80% of urothelial carcinoma may be identified on H & E alone, however many cases are difficult due to a broad diversity of microscopical morphologies and overlapping with direct invasion and metastases from other locations, notably genitourinary. Plasmacytoid, micropapillary, sarcomatoid, and small cell urothelial carcinomas are aggressive and have poor outcomes. Recognizing these mutations allows aggressive therapy that varies from conventional urothalial cancer.[6] Many immunohistochemical markers can differentiate urothelial carcinoma from metastatic tumours, although they have limited sensitivity and specifity. Uroplakin III has high specifity but poor

sensitivity, while p63, S-100, and thrombomodulin have high sensitivity but low specifity since they are not confined to urothelial cancer. GATA3, with or without additional IHC panels, has a positive of 67–90%. However, the proportion and intensity may vary in various variations and stages of primary and metastatic urothelial carcinoma.[7] Higgins et al. explored this marker for the first time in 2007.[10] In this study, we applied GATA3 antibody to all 90 cases, including 70 cases of urothelial carcinoma, 10 cases of prostatic adenocarcinoma, and 10 cases of renal cell carcinoma. The sensitivity was 84.3% (59 cases) of urothelial carcinoma, which was similar to Oh WJ et al[11] 84.8%, Naik M et al[7] 79.5%, Miettinen M, et al[12] 90%, but different from Leivo M et al[13] 99% and Mohammed K et al 70.5%.[6] Extremely significant association was reported between GATA3 expression and tumour grade (P value < 0.001), with 94% of low-grade tumours expressing GATA3 compared to 74% of high-grade tumours. These results are similar to Naik M et al[7], where high-grade cases were 78% and low-grade positivity was 100%, although the number of cases in the aforementioned study was 116 and only 6 were low-grade. Rana C et al[2] found 100% Few studies like Hoang L et al[14] revealed no significant link between grade and intensity of GATA3 expression, with 84% and 83% expression for low-grade and high-grade tumours, respectively. This may be due to the scoring system used to calculate positive. Regarding tumour stage, there was a significant correlation (P value =0.003): 97% of non-muscle invasive urothelial carcinoma (Ta and T1) were positive, while 70.5% of muscle-invasive (T2, T3, and T4) were positive. Muscle-invasive tumours showed weak to moderate positivity, while non-invasive tumours showed moderate to strong positivity. Similar correlations were found in Rana C et al[2], who found 87% positivity in non-muscle invasive urothelial carcinoma compared to 66% in muscle invasive tumours, Naik M et al[7], who found 100% positivity versus 73% in muscle invasive cases, and Miyamoto H et al[15] who found 98% positivity in non-muscle invasive and 72% in muscle invasive. Recent studies have linked GATA3 to tumour stage and grade as a prognostic factor. Miyamoto et al[15] was the first to include stage and grade as prognostic parameters, as GATA3 significantly decreased with higher grade and/or stage. However, strong expression was an independent factor for poor prognosis, especially in males with muscle-invasive tumours. Kamel N.[16] Regarding other histopathological parameters like number of mitoses per 10HPF, no significant correlation was found (P value=0.2), in contrast to Rana C et al[2] who found a significant correlation between number of mitoses and decrease in GATA3 positivity (p value =0.001). No other study was found regarding this correlation, but some studies included proliferative index Ki67 along with GATA3 expression, Kamel N et al[17] show no significant correlation. Urothelial carcinoma molecular subtypes, proliferation count methodologies, and no major research may explain these variances. Our study found no significant correlation between GATA3 positivity and necrosis (P value = 0.19), contrary to Rana C et al.[2], but no other studies were found on this parameter. Necrosis is usually associated with higher tumour grade and stage[18], so further studies may clarify the importance of this parameter. This study demonstrated a highly significant connection (P < 0.01) between GATA3 positivity in 84.3% of urothelial carcinoma and GATA3 negativity in all prostatic adenocarcinomas. In Iraq, Abdullah W et al.[19] compared GATA3 sensitivity between urothelial carcinoma and prostatic adenocarcinoma, finding 96% sensitivity for the former and no positives for the latter. All research yielded the same findings.[20,21] Miettinen M et al.[12] discovered that 2% of prostatic adenocarcinomas were GATA3-positive in 2500 epithelial and mesenchymal tumours. GATA3 was found to be a sensitive marker for distinguishing urothelial carcinoma from papillary and clear cell renal cell carcinoma in all studies (P value < 0.001).[22] GATA3 is positive in 50% of chromophobe RCC, 70% of papillary clear cell RCC, and uncommon in other types.[12]

CONCLUSION

To verify urothelial lineage, GATA3 may serve as a sensitive and specific marker. Applied in the right clinical context, it is a reliable marker. GATA3 expression was strongly linked to both the grade and stage of urothelial carcinoma, suggesting that it may be useful not only as a diagnostic but also as a prognostic marker.

REFERENCES

1. Cancer today [Internet]. Gco.iarc.fr. 2020 [cited 2 May 2020]. Available from: https://gco.iarc.fr/today/fact-sheets-populations.
2. Rana C, Agarwal H, Babu S, Kumar M, Singhai A, Shankhwar S et al. Diagnostic utility of GATA3 immunohistochemical expression in urothelial carcinoma. Indian Journal of Pathology and Microbiology, 2019; 62(2): 244.
3. Zhou M, Magi_Galluzi C. Genitourinary Pathology. 2nd ed. 2015. Pages 181 to 247.
4. Rosai J, Ackerman L, Goldblum J, Lamps L, McKenney J, Myers J. Rosai and Ackerman's surgical pathology. Philadelphia: Elsevier, 2018; Pages 1073 to 1079.
5. Szymanska K, T Bosman, F, Hainaut P. Bladder Cancer: Pathology, Genetics, Diagnosis, and Treatment. Elsevier, 2019.
6. Mohammed K, Siddiqui M, Cohen C. GATA3 immunohistochemical expression in invasive urothelial carcinoma. Urologic Oncology: Seminars and Original Investigations, 2016; 34(10): 432.e9-432.e13.
7. Naik M, Rao B, Fonseca D, Murthy S, Giridhar A, Sharma R et al. GATA-3 Expression in all Grades and Different Variants of Primary and Metastatic

Urothelial Carcinoma. Indian Journal of Surgical Oncology, 2020.
8. Remmele W, Stegner HE: Recommendation for uniform definition of an immunoreactive score (IRS) for immunohistochemical estrogen receptor detection (ER-ICA) in breast cancer tissue. Pathol, 1987; 8: 138–140.
9. Krajewska M, Krajewski S, Epstein JI, Shabaik A, Sauvageot J, Song K, Kitada S, Reed JC: Immunohistochemical analysis of bcl-2, bax, bcl-X, and mcl-1 expression in prostate cancers. Am J Pathol, 1996; 148: 1567– 1576.
10. Higgins J, Kaygusuz G, Wang L, Montgomery K, Mason V, Zhu S et al. Placental S100 (S100P) and GATA3: Markers for Transitional Epithelium and Urothelial Carcinoma Discovered by Complementary DNA Microarray. The American Journal of Surgical Pathology, 2007; 31(5): 673-680.
11. Oh W, Chung A, Kim J, Han J, Hong S, Lee J et al. Differential Immunohistochemical Profiles for Distinguishing Prostate Carcinoma and Urothelial Carcinoma. Journal of Pathology and Translational Medicine, 2016; 50(5): 345-354.
12. Miettinen M, McCue PA, Sarlomo-Rikala M, et al. GATA3: a multispecific but potentially useful marker in surgical pathology: a systematic analysis of 2500 epithelial and nonepithelial tumors. Am J Surg Pathol, 2014; 38(1): 13-22.
13. Leivo M, Elson P, Tacha D, Delahunt B, Hansel D. A combination of p40, GATA-3 and uroplakin II shows utility in the diagnosis and prognosis of muscle-invasive urothelial carcinoma. Pathology, 2016; 48(6): 543-549.
14. Liu H, Shi J, Wilkerson M, Lin F. Immunohistochemical Evaluation of GATA3 Expression in Tumors and Normal Tissues. American Journal of Clinical Pathology, 2012; 138(1): 57-64.
15. Miyamoto H, Izumi K, Yao J, Li Y, Yang Q, McMahon L et al. GATA binding protein 3 is down-regulated in bladder cancer yet strong expression is an independent predictor of poor prognosis in invasive tumor. Human Pathology, 2012; 43(11): 2033-2040.
16. Kamel N, Abdelzaher E, Elgebaly O, Ibrahim S. Reduced expression of GATA3 predicts progression in non–muscle invasive urothelial carcinoma of the urinary bladder. Journal of Histotechnology, 2019; 43(1): 21-28.
17. Inoue S, Mizushima T, Fujita K, Meliti A, Ide H, Yamaguchi S et al. GATA3 immunohistochemistry in urothelial carcinoma of the upper urinary tract as a urothelial marker and a prognosticator. Human Pathology, 2017; 64: 83-90.
18. Zhang, X., Zhang, Z., Yang, P., Cai, M., Hu, W., Yun, J., Zhou, F., Qian, C. and Cao, Y., 2015. Tumor necrosis predicts poor clinical outcomes in patients with node-negative upper urinary tract urothelial carcinoma. Japanese Journal of Clinical Oncology, 45(11): 1069-1075.
19. Paner G, Annaiah C, Gulmann C, Rao P, Ro J, Hansel D et al. Immunohistochemical evaluation of novel and traditional markers associated with urothelial differentiation in a spectrum of variants of urothelial carcinoma of the urinary bladder. Human Pathology, 2014; 45(7): 1473-1482.
20. Hoang L, Tacha D, Bremer R, Haas T, Cheng L. Uroplakin II (UPII), GATA3, and p40 are Highly Sensitive Markers for the Differential Diagnosis of Invasive Urothelial Carcinoma. Applied Immunohistochemistry & Molecular Morphology, 2015; 23(10): 711-716.
21. Chang, A., Amin, A., Gabrielson, E., Illei, P., Roden, R. B., Sharma, R., & Epstein, J. I. (2012). Utility of GATA3 immunohistochemistry in differentiating urothelial carcinoma from prostate adenocarcinoma and squamous cell carcinomas of the uterine cervix, anus, and lung. The American journal of surgical pathology, 36(10): 1472–1476.
22. Chang, A., Brimo, F., Montgomery, E. and Epstein, J., 2013. Use of PAX8 and GATA3 in diagnosing sarcomatoid renal cell carcinoma and sarcomatoid urothelial carcinoma. Human Pathology, 44(8): pp.1563-1568.