40 yaş altı mesane tümörlerinde orta dönem takip sonuçlarımız

Our mid-term follow-up results in bladder tumors below 40 years of age

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Özet

Amaç: Ürotelyal tümörler genç hastalarda nadiren görülür. Bu nedenle genç hastalarda hastalığın doğal seyri ile ilgili bilgiler net değildir ve bu kategoride değerlendirilecek hastalar henüz tanımlanmamıştır. Çalışmamızda, küçük serilerimize dayanarak genç hastalarda görülen mesane tümörünün doğal seyrini öngörmeyi amaçladık.

Gereç ve Yöntemler: Ocak 2012 ile Ocak 2017 arasında üroloji kliniğine başvuran 18-40 yaşları arasındaki toplam 15 hasta geriye dönük olarak değerlendirildi. Olgularımız demografik veriler (yaş ve cinsiyet), sigara öyküsü, tümör tipi, grade, evre, odak sayısı, tümör rekürrensi ve intravezikal tedavi parameterleri değerlendirilerek 30 yaş altı ve 30-40 yaş aralığı olmak üzere iki ayrı gruba ayrılayarak analiz edildi

Bulgular: Olgularımız 30 yaşın altındaki (n = 7; % 46.7) veya üzeri (n = 8; % 53.3) idi. Otuz yaşın altındaki düşük dereceli tümörlerin oranları 30 yaşın üzerindeki yaş grubuna göre daha yüksek bulundu (p: 0.007; p <0.01).

Sonuç: Çalışmamızda, hastalar < 30 ve > 30 yaş hastalar olarak değerlendirildiğinde, yaş faktörünün, tümör boyutu, histopatolojik grade ve evre, intravezikal tedaviye verilen tedavi yanıtları ve tümör rekürrensi ile doğrudan korelasyona sahip potansiyel olarak negatif bir prediktif faktör olduğu gözlemlendi.

Anahtar Kelimeler: Mesane tümörü, genç hasta, tümör rekürrensi

Abstract

Purpose: Urothelial tumors are rarely seen in young patients. Therefore in these types of patients, information related to natural course of the disease are not clear-cut and patients who will be evaluated in the young age category have not been defined yet. In our study, based on our small series, we aimed to predict the natural course of the bladder tumor seen in young patients peculiar to this age group.

Material and Methods: A total of 15 patients aged between 18-40 years who consulted to our urology clinic between January 2012 and January 2017 were retrospectively evaluated. Our cases were analyzed by demographic data (age and gender), smoking history, tumor type, grade, stage, number of foci, tumor recurrence and intravesical treatment parameters and dividing into two groups of under age 30 and age range 30-40 years.

Results: Our cases were either below (n=7; 46.7 %) or above (n=8; 53.3 %) 30 years of age. The rates of low grade tumors in the age group of ≤ 30 years were found to be higher when compared with the age group of > 30 years (p:0.007; p<0.01).

Conclusion: In our study, when patients were evaluated as those aged < 30 and > 30 years, age factor was observed to be a potentially negative predictive factor directly correlated with tumor size, histopathological grade and stage, treatment responses to intravesical therapy and tumor recurrence.

Keywords: Bladder tumors, young patients,tumor recurrence

INTRODUCTION

Urothelial tumors are usually seen in elderly people, with a male predominance. The median ages of patients at the time of the initial diagnosis are 69 in men and 71 in women [1]. Urothelial tumors are rarely seen in young patients. When studies on this issue have been analyzed, the definition of young age has usually been used for patients aged between 20-40 [2,3]. For the definition of 'young age bladder tumor' use of different age intervals in various studies has resulted in acquirement of inconsistent relevant data. Some studies have reported that younger patients with urothelial tumors had more favorable prognosis than older patients. However, other studies have shown that the clinical course of the disease in younger patients is similar to that in older patients [4,5]. In our study we comparatively evaluated the patients aged 18-40 years old diagnosed with a bladder tumor with respect to age and tumor size.

MATERIAL AND METHODS

A total of 15 patients visiting our clinic between January 2012 and January 2017 were evaluated retrospectively. The patients were analyzed according to demographic data (age, gender), smoking history, type, size, stage and grade of the tumor, number of tumor foci, tumor recurrence, up/down- grading/staging and intravesical therapy. All of the surgical specimens were examined by a dedicated genitourinary pathologist and processed according to standardized procedures. The tumor grade was determined according to the 2004 World Health Organization classification system and the histopathologic stage was determined according to the 2010 American Joint Committee on Cancer staging system. The Transurethral resection (TUR) was performed as initial treatment of choice for non-muscle invasive bladder cancer (NMIBC). The EAU recommendations to be followed up in patients after TUR of NMIBC were applied (Patients with Ta/T1 tumors at low risk of recurrence and progression should have a cystoscopy at 3 months. If negative, the following cystoscopy is advised 9 months later, and then yearly for the next 5 years. Patients with Ta/T1 tumors at high risk of progression and those with CIS should have a cystoscopy and urinary cytology at 3 months. If negative, the following cystoscopy and cytology should be repeated every 3 months for a 2-year period and every 6 months thereafter for a 5-year period, and then yearly. Yearly imaging of the upper tract is recommended.).

Statistical Analyses: For statistical evaluation of study data, IBM's SPSS Statistics 22 (IBM SPSS) program was used. In addition to descriptive statistical methods (means, standard deviation, frequency) for the comparison of qualitative data, Fisher's Exact test *chi*-square test and Fisher –Freeman- Halton Test were used and the Level of significance was accepted a p value of <0.05.

RESULTS

Our study was performed on a total of 15 cases including 11 (73.3 %) male and 4 (26.7 %) female patients. Mean age of the patients was 32.13±7.81 (range18-40 years) years. The Patients were either older (> 30 yrs; n=8; 53.3) or younger (< 30 yrs n=7; 46.7 %). Twelve (80 %) of the patients were smokers. Medical anamnesis of the patients did not reveal any evidence of comorbidity or surgical intervention.

Single (n=9; 60 %) and multiple (n=6; 40 %) tumor foci were detected in a respective number of patients. In our patients, tumors were either larger (n=7; 46.7 %) or smaller (n=8; 53.3 %) than 3 cm in diameter. Distribution of the cases based on histopathology results were as follows: papillary urothelial neoplasia of low malignancy potential (PUNLMP) (n=2; 13.3 %), T1 high grade (HG) (n=2, 13.3 %), T1 low grade (LG) (n=5; 33.3%), T2 high grade (n=1; 6.7 %) and Ta low grade (n= 5; 33.3 %). In only one case older than 30 years of age with a tumor size smaller than 3 cm, in situ carcinoma was seen. Median follow-up period was 22.4 months (range, 4-35 months). Eight patients, whose histopathology results were reported as T1 and T2, underwent re-TUR one month later. All the patients took a single dose of 40 mg mitomycin as an intravesical instillation during the postoperative period. A patient older than 30 years of age with T2 high grade underwent cystectomy. Two cases with histopathology results, reported as PUNLMP, didn't undergo intracavitary induction therapy and no tumor recurrence was observed (Table 1). Twelve (80 %) patients underwent intravesical therapy. Induction therapy was applied to Ta patients with 30 mg mitomycin-C, while T1 patients re-

Table 1: Distribution of study data

		n	%
Pathology	**PUNLMP [1]**	2	13,3
	T1 HG[2]	2	13,3
	T1 LG[3]	5	33,3
	T2 HG[2]	1	6,7
	Ta LG[3]	5	33,3
In Situ Carcinoma	**Present**	1	6,7
	Absent	14	93,3
Tumor size	**>3 cm**	7	46.7
	<3 cm	8	53.3
Recurrences	**Present**	6	40
	Absent	9	60
Smoking	**Yes**	12	80
	No	3	20
Number of tumor foci	**Multiple**	6	40
	Single	9	60
Intravesical Therapy	**Applied**	12	80
	None	3	20

PUNLMP[1]: papillary urothelial neoplasia of low malignancy potential, HG[2]: High grade, LG[3]: Low grade

ceived intravesical Bacille Calmette-Guérin (BCG) therapy for 6 weeks. Recurrences were seen in 40 % (n=6) of these cases. The patients who demonstrated recurrences included 4 cases with T1 aged > 30 years, T1 (n=1) and Ta (n=1) patients younger than 30 years of age. Among the cases with recurrences, evidence of upstaging and upgrading (n=1; T1 LG to T2 HG), upstaging (n=1; Ta LG to T1 LG) and down staging (n=1; T1 LG to Ta LG) were observed. The patient older than 30 years of age with recurrences, together with tumor upstaging and upgrading, underwent cystectomy. All of the remaining patients were once more started on intracavitary induction therapy, followed by maintenance therapy completed within 12 months. During the follow-up period, any recurrence was not observed.

When our patients were evaluated in two age categories as younger and older than 30 years of age, any statistically significant difference was not detected with respect to gender of the patients (p>0.05). However, a statistically significant difference was detected between histopathology results based on age groups (p:0.044; p<0.05). We performed pairwise comparisons to determine the source of significance in data and, in the age group of patients younger than 30 years of age, the number of low- stage and low-grade tumors were significantly higher when compared with the older age group (p:0.007; p<0.01). Rates of other histopathological types of tumors did not statistically significantly differ between both groups (p>0.05). Any statistically significant difference was not detected between both age categories with respect to tumor size, recurrence rates, smoking status and number of tumor foci (for all, p>0.05) (Table 2).

Urinary system ultrasonograms were performed as initial work-up in patients with hematuria and 11 of 15 patients' ultrasonograms reported an abnormality in the bladder (increased bladder wall thickness, papillary tumor, calcification and etc.). Urine cytology was obtained from the other 4 of 15 patients to establish malignant urothelial cells but only one patient's cytology was positive. 3 patients with a normal ultrasonography report and negative urine cytology underwent diagnostic cystoscopy because of recurrent microscopic hematuria.

Distribution of genders among our patients based on tumor sizes could not reveal any statistically significant intergroup differences (p>0.05). Still, a statistically significant difference was not found in distribution of histopathology results based on tumor size (p>0.05). The recurrence rates based on tumor size were not statistically significantly different (p:0.041; p<0.05). Median recurrence rate in cases with tumor size larger than 3 cm was significantly higher than those cases with smaller tumors (12.5 %). Rates of cigarette smoking did not statistically significantly differ according to tumor size (p>0.05). A statistically significant difference was found between tumor size and number of tumor foci (p:0.041; p<0.05). Multiple foci was seen in significantly higher number of (71. %) tumors larger than 3 cm in diameter when compared with smaller tumors (12.5 %) (Table 3).

DISCUSSION

Urothelial carcinoma is seen in 1 and 2.4 % of the patients within four decades of their lives, while it is seen in only 0.1-0.4 % of the patients aged below 20 years [3,6]. In

Table 2: Evaluation of some characteristics of age groups

		Age group		p
		>30 (n=8)	≤ 30-40 (n=7)	
		n (%)	n (%)	
Gender	**Female**	1 (12.5%)	3 (42.9%)	**0.282**
	Male	7 (87.5%)	4 (57.1%)	
Histopathology	**PUNLMP[1]**	1 (12.5%)	1 (14.3%)	**0.030***
	T1 HG[2]	2 (25%)	0 (0%)	
	T1 LG[3]	4 (50%)	1 (14.3%)	
	T2 HG[2]	1 (12.5%)	0 (0%)	
	Ta LG[3]	0 (0%)	5 (71.4%)	
Tumor Size	**>3 cm**	5 (62.5%)	2 (28.6%)	**0.315**
	<3 cm	3 (37.5%)	5 (71.4%)	
Number of recurrences		4 (50%)	2 (28.6%)	**0.608**
Smoking		7 (87.5%)	5 (71.4%)	**0.569**
Number of tumor foci	**Multiple**	3 (37.5%)	3 (%42.9)	**1.000**
	Single	5 (62.5%)	4 (57.1%)	
Intravesical Therapy		6 (62.5%)	6 (71.4%)	**1.000**

*Fisher's Exact Test, and Fisher- Freeman- Halton Test were used *p<0.05.* PUNLMP[1]: papillary urothelial neoplasia of low malignancy potential, HG[2]: High grade, LG[3]: Low grade

the current study, all patients were 40 years old or younger at the time of initial diagnosis, with a mean age of 32.1 years. In our series, male/female ratio was 2.75:1. In adult patients this ratio was reported as 4:1 [2].

Though oncogenesis of urothelial tumors is not clear-cut in young patients, various environmental and genetic factors have been blamed in the etiology. The most important risk factor known in adult patients with bladder tumors is smoking which is also valid for young patients. This risk is directly proportional to the duration of smoking. In a study performed, 67 % of the bladder cancer patients aged <30 years had a smoking history and in the same study 95 % of the patients aged 30-40 years were indicated as smokers [7]. However in our study, smoking rates were detected to be 87.5 and 71.4 % for patients younger and older than 30 years of age, respectively. All of our smoking patients stopped smoking after pathological diagnosis of bladder cancer. Occupational exposure is another known risk factor for urothelial tumors in old patients, but its role is uncertain in young patients. One of our patients had occupational exposure (worked in a leather factory for 2 years) that might be related to urothelial carcinogens. Genetic changes frequently seen in older patients with bladder tumors could not be observed in young patients. However, it has been suggested that genetic factors might play significant roles at the early stages of bladder tumor observed in young patients [7].

The most common presenting symptom of bladder cancer is painless macroscopic hematuria, which occurs in about 85% of patients and the second most common presenting symptoms are bladder irritability, urinary frequency, urgency and dysuria. All of our patients presented with macroscopic hematuria.

The pathologic diagnosis is often delayed in young patients because clinical suspicion of urothelial tumors is generally low for this age group [8]. Several benign papillary lesions of the urinary bladder, such as polypoid cystitis and nephrogenic adenomas, should be differentiated from papillary urothelial carcinomas. However, it is unclear whether it resulted from a genetic predisposition or common environmental exposure among family members [9,10].

In a comparative study performed, only 3.0% of bladder cancer patients younger than 30 years of age had muscle–invasive disease and only 1.7% of them had a high–grade tumor. In our study, high- grade disease was not detected in patients younger than 30 years of age, while one of our cases was evaluated as T1 low- grade tumor. Yossepowitch and Dalbagni found no difference in grade or stage upon comparing 74 patients <40 years of age with 75 patients >65 years of age [4]. It was evident that during the first two decades of their lives, these patients had harbored relatively indolent bladder cancer [11]. Nevertheless, aggressive bladder cancer has been reported in 31

Table 3: Assessments based on tumor size

		Tumor size		p
		>3 cm (n=7)	< 3 cm (n=8)	
		n (%)	n (%)	
Gender	**Female**	1 (14.3%)	3 (37.5%)	**0,569**
	Male	6 (85.7%)	5 (62.5%)	
Histopathology	**PUNLMP[1]**	0 (0%)	2 (25%)	**0.176**
	T1 HG[2]	1 (14.3%)	1 (12.5%)	
	T1 LG[3]	4 (57.1%)	1 (12.5%)	
	T2 HG[2]	1 (14.3%)	0 (0%)	
	Ta LG[3]	1 (14.3%)	4 (50%)	
Number of recurrences		5 (71.4%)	1 (12.5%)	**0.041***
Smoking		6 (85.7%)	6 (75%)	**1.000**
Number of tumor foci	**Multiple**	5 (71.4%)	1 (12.5%)	**0.041***
	Single	2 (28.6%)	7 (87.5%)	
Intravesical Therapy		6 (71.4%)	6 (62.5%)	**1.000**

*Fisher's Exact Test, and Fisher- Freeman- Halton Test were used *p<0.05.* PUNLMP[1]: papillary urothelial neoplasia of low malignancy potential, HG[2]: High grade, LG[3]: Low grade

months [12] and a 14 year- old children [13].

CONCLUSION

When we review the literature, for each decade passed, we observe progression of the grade and stage of the bladder tumor. When we take the results of our study into consideration, we think that, especially for the definition of young-age bladder tumor, the cut-off age of 30 years carries utmost importance. We are of the opinion that the patients younger than 30 years of age demonstrate improved treatment response and prognosis and the patients older than 30 years of age should be evaluated in the same category with adult patient group regarding prognosis of the disease.

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