

## Adolesan ve genç erişkinlerdeki ürotelyal mesane neoplazmları

### *Urothelial neoplasms of urothelial bladder in adolescent and young adult patients*

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#### Özet

**Amaç:** Mesane tümörleri adolesan ve genç erişkinlerde nadir görülür. Literatürdeki çalışmalarda, genellikle bu yaş gruplarında sadece ürotelyal karsinomlar araştırılmıştır. Biz bu çalışmada, adolesan ve genç erişkinlerde görülen bütün ürotelyal mesane tümörlerini, tanı, tedavi ve prognoz açısından araştırmayı amaçladık.

**Hastalar ve Metod:** Çok merkezli bu retrospektif çalışmada, 2008 ile 2014 yılları arasında tedavi edilen hastalar incelendi. Kırk yaş altındaki 42 hasta çalışmaya alındı. Mesane tümörleri ultrasonografi ve sistoskopi ile tanımlandı ve transüretral mesane rezeksiyonu (TUR-M) ile tedavi edildi.

**Bulgular:** Hastaların ortalama yaşı 24.21 ±10.137 (12-24) idi. Otuz iki (%71,4) hasta makroskopik hematüri ile başvurdu. Hastaların patolojik spesmenleri şu şekilde raporlandı; 5 hastada nadir benign lezyon, 5 hastada papillom, 6 hastada düşük malignite potansiyelli ürotelyal neoplazm, 21 hastada düşük grade ürotelyal karsinom ve 5 hastada yüksek grade ürotelyal karsinom. İki hastada kas invaziv mesane kanseri vardı (pT2). Düzenli sistoskopik takipler sırasında 5 (%11,9) hastada tümör nüksü meydana geldi.

**Sonuç:** Adolesan ve genç erişkinlerdeki mesane tümörlerinin yaklaşık %40'ı ürotelyal karsinom dışı tümörlerdir. Bu tümörlerin çoğu benign karakterde olmasına rağmen nüks etme potansiyelleri az değildir. Adolesan ve genç erişkinlerde, ürotelyal karsinomlarda olduğu gibi karsinom dışı tümörlerin de yakından takip edilmesi gerektiğini düşünüyoruz.

**Anahtar Kelimeler:** benign tümörler, adolesan, hastalık yönetimi, mesane kanseri

#### Abstract

**Objectives:** Bladder tumors are rare in adolescent and young adult patients. To date, urothelial carcinomas have usually been the only tumors investigated in these age groups. In this study, we aimed to describe the diagnosis, treatment, and prognosis of all urothelial bladder tumors in adolescent and young adult patients.

**Materials and Methods:** This was a retrospective multicenter study involving patients who were treated between 2008 and 2014. Forty-two patients aged less than 40 years were enrolled in the study. Bladder tumors were diagnosed using ultrasonography and cystoscopy, and treated through transurethral resection of the bladder (TURBT).

**Results:** The mean age of the patients was 24.21 ±10.137 years (range, 12-40 years). Thirty (71.4%) of the 42 patients were admitted with gross hematuria. The pathology of all patients was reported as follows: 5 with uncommon benign lesions, 5 with papilloma, 6 with papillary urothelial neoplasm of low malignant potential (PUNLMP), 21 with low-grade urothelial carcinoma, and 5 with high-grade urothelial carcinoma. Two patients had muscle invasive bladder cancer (pT2). Relapse was observed in 5 (11.9%) patients during regular cystoscopic follow-up.

**Conclusion:** Approximately 40% of the bladder tumors in adolescent and young adult patients were not urothelial carcinomas. The majority of these tumors were benign tumors but relapse was not less frequent in these tumors. We suggest that urothelial benign tumors and urothelial carcinomas of the bladder should be closely monitored in adolescent and young adult patients.

**Keywords:** benign neoplasms; cancer; adolescent; disease management; follow-up

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**Table 1.** The demographic characteristics of the patients

Patients (n)	42
Mean age (range), yr.	24.21 (12-40)
Males/females, n (%)	27/15 ( 64.3 /35.7)
Mean follow-up (range), yr.	5.1 (2-9)
Recurrence rate, n (%)	5 (11.9)
Clinical characteristics at presentation, n (%)	
Gross Hematuria	30 (71.4)
Dysuria	1 (2.4)
Abdominal Pain	2 (4.8)
Incidental	4 (9.5)
Undefined	5 (11.9)

**Table 2.** Detailed pathologic characteristics and recurrence rates of bladder urothelial tumors

Pathologic characteristics	N (%)	Recurrence, n (%)
Uncommon benign lesions	5 (11.9)	
polypoid cystitis	1 (2.4)	1 (2.4)
nephrogenic adenoma	2 (4.8)	2 (4.8)
squamous metaplasia	1 (2.4)	
granulomatous cystitis	1 (2.4)	
Papilloma	5 (11.9)	
urothelial papilloma	4 (9.5)	
inverted papilloma	1 (2.4)	
PUNLMP*	6 (14.3)	1 (2.4)
Urothelial carcinoma, low grade	21 (50)	1 (2.4)
Ta, stage	12 (28.6)	
T1, stage	9 (21.4)	
Urothelial carcinoma, high grade	5 (11.9)	
T1, stage	3 (7.1)	
T2, stage	2 (4.8)	
Total	42	5 (11.9)

\*PUNLMP= Papillary urothelial neoplasm of low malignant potential

**Introduction**

Bladder tumors (BT) are the most common tumors of the urinary tract, and bladder cancers constitute most of these tumors. Bladder cancer is the seventh most common cancer in men and the seventeenth most common cancer in women. The worldwide age-standardized inci-

dence rate is 9 per 100000 for men and 2 per 100000 for women (2008 data).<sup>[1]</sup> Despite these high rates in the general population, it is rare in adolescent and young adult patients. In the prevailing opinion, these tumors have a low grade of malignancy, show little tendency toward recurrence, and have a good prognosis.<sup>[2-4]</sup> However, earlier studies have generally only focused on urothelial carcinomas of the bladder. We think that tumor recurrence is no less frequent in benign bladder tumors.

In our previous study, we reported the clinicopathologic characteristics of urothelial bladder tumors in patients aged less than 18 years.<sup>[5]</sup> In this multicenter study, we made a detailed investigation of urothelial bladder tumors in patients aged less than 40 years. We aimed to describe the presentation, diagnostic methods, treatment, pathologic examination, and follow-up methods of all bladder urothelial tumors of patients in this age group.

**Material and Methods**

By means of a retrospective multicenter study (3 centers), we identified 42 urothelial bladder tumors in adolescent patients and adults aged less than 40 years that were diagnosed between 2006 and 2014. This study was prepared in accordance with the Declaration of Helsinki. Written informed consents were taken from all patients.

A detailed history was taken from all patients and pediatric patients' parents. The initial diagnosis of bladder tumor was confirmed using ultrasonography or cystoscopy. After the initial diagnosis, each patient underwent transurethral resection of the bladder tumor (TURBT) for a definitive diagnosis and treatment. Similarly, each patient's cystoscopy and ultrasonography was reviewed every six months during the first year and once a year in subsequent years of the follow-up. Radical cystectomy with urinary diversion was performed in two patients whose initial tumor stage was pT2.

**Table 3.** Tumor recurrence and progression in patients with non-muscle-invasive urothelial tumors according to European Organization for Research and Treatment of Cancer (EORTC) risk group stratification

Risk group stratification	N (%)	Mean follow-up (range), yr.	Progression rate	Recurrence rate n (%)	p value
Low-risk tumors	14 (45.2)	5 (2-7)	0	1 (7.1)	>0.05
Intermediate-risk tumors	4 (12.9)	5 (2-6)	0	0	
High-risk tumors	13 (41.9)	5.2 (2-9)	0	1 (7.7)	
Total	31 (100)	5.1 (2-9)	0	2 (6.5)	

**Figure 1.** Histopathologic images of some non-urothelial carcinomas. A. Polypoid cystitis demonstrating intense edema in sub-epithelial area (H&E, x40). B. Nephrogenic adenoma with tubular structures covered by flattened and cuboidal epithelium forming a nephrogenic adenoma (H&E, x100). C. Urothelial papilloma showing a papillomatous structure composed of urothelial epithelium. The surrounding edematous stroma includes congestive vascular structures (H&E, X10). Inverted papilloma containing areas showing inverted growth patterns and anastomosing with each other beneath the surface epithelium (arrow) (H&E, x100).

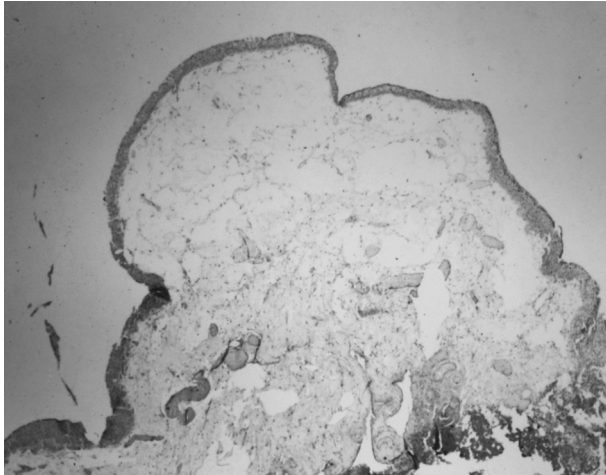


Figure 1A.

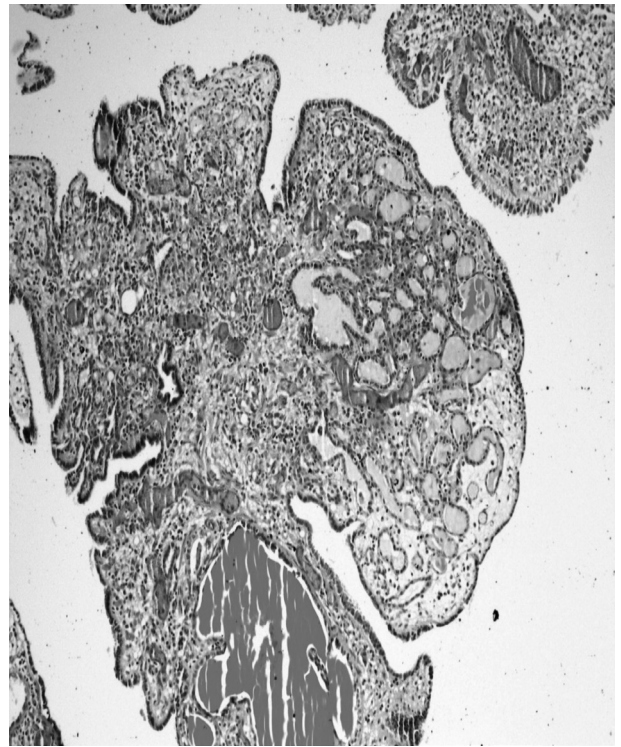


Figure 1C.

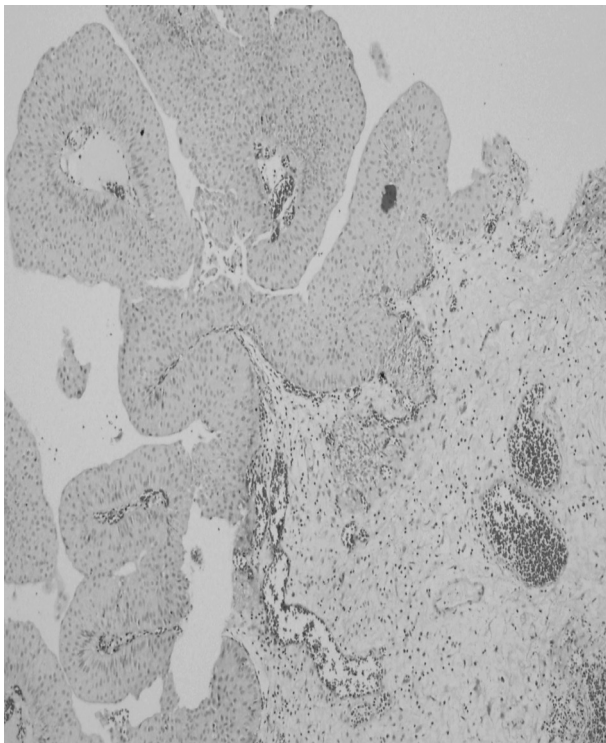


Figure 1B.

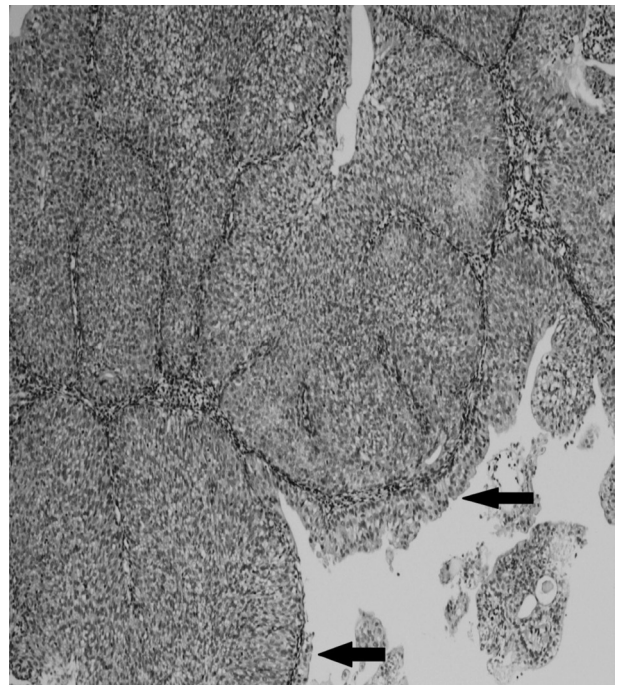


Figure 1D.

### Statistical Analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) for Windows version 17.0. Categorical variables were described as frequency (percentage), and mean  $\pm$  standard deviation were used for continuous parameters. Categorical variables were compared between two or more groups using the Chi-square test. For all analyses,  $p < 0.05$  was considered statistically significant.

### Results

The patients' demographic characteristics and clinical characteristics at presentation are described in Table 1. The mean age of patients (16 adolescents and 26 young adults) was  $24.21 \pm 10.137$  years (range, 12-40 years) and the patients' main symptom was hematuria (71.4%). Tumor recurrence occurred in 5 (11.9%) patients during follow-up.

Initial tumor diagnosis was made using ultrasonography in 40 patients and with cystoscopy in 2 patients; ultrasonography was normal in these two patients. After the initial diagnosis, TURBT was performed under general or regional anesthesia.

Detailed pathologic characteristics and recurrence rates of bladder urothelial tumors are shown in Table 2. The pathology specimens of the patients were reported as uncommon benign lesions, papilloma, PUNLMP, low-grade urothelial carcinoma, and high-grade urothelial carcinoma with a frequency of 5, 5, 5, 21, and 5, respectively. (Fig.1)

Superficial urothelial neoplasms were classified in accordance with the World Health Organization/International Society of Urological Pathology (WHO/ISUP) 2004 histologic classification;<sup>[6]</sup> 5 patients were found to have papilloma, 6 had papillary urothelial neoplasm of low malignant potential (PUNLMP), 12 had low-grade pTa, 9 had low-grade pT1, and 3 had high-grade pT1.

The mean follow-up time for the patients was 5.1 years (range, 2-9 years). Relapse was observed in five patients with bladder tumor during follow-up. Relapse occurred in both patients who were diagnosed as having nephrogenic adenoma. Nephrogenic adenoma relapsed once in one patient and twice in another during an average 4.5 years of follow-up. Relapse occurred once in one patient with polypoid cystitis, one with PUNLMP, and one with low-grade pT1 urothelial carcinoma. Tumor recurrence and progression in patients with non-muscle-invasive urothe-

lial neoplasm are shown in Table 3. These were defined in accordance with the European Organization for Research and Treatment of Cancer (EORTC) risk group stratification, which was subsequently implemented in the European Association of Urology guidelines.<sup>[7]</sup> According to the EORTC risk group stratification, there was no statistical difference between the groups in terms of tumor recurrence and progression. Tumor progression did not occur in any patients. The final pathologic examination of the two patients who underwent radical cystectomy revealed pT2a N0 urothelial carcinoma. All patients are alive.

### Discussion

Although bladder tumor is seen in all age groups, it is rare in younger patients, especially in adolescents. Diagnosis is sometimes delayed, probably because of the rarity of this disease and the predominance of benign causes of hematuria in these age groups.<sup>[5,8]</sup> When bladder cancer is seen in younger patients, it becomes the focus of attention.

Publications that reported bladder tumors in adolescent and young adult patients generally only consist of urothelial bladder cancer.<sup>[9-11]</sup> However, as seen in our patients, the portion of bladder tumors that is benign is not less in this age group. To our knowledge, no studies have examined benign bladder tumors in detail in adolescent and young adult patients. Approximately 60% of patients in our study had urothelial carcinoma (low-grade and high-grade urothelial carcinoma), but the other 40% had different histopathologic features (see Table 2). Some of these tumors, nephrogenic adenoma for example, are benign tumors, are rarely seen, but may recur often. Therefore, these tumors and urothelial carcinomas should be closely monitored.

Nephrogenic adenoma is a rare benign tumor of the urothelium that is believed to result from metaplasia arising from chronic irritation.<sup>[12]</sup> Recurrence of nephrogenic adenoma is very common, but a malignant transformation has not been reported to date. Both of our patients had tumor recurrence.

Polypoid cystitis is defined as a nonspecific mucosal reaction secondary to chronic bladder inflammation.<sup>[13]</sup> Although indwelling catheter is the main recognized cause of polypoid cystitis, some case reports unrelated to catheterization have been described.<sup>[14,15]</sup> There was a history of long-term catheterization in our patient.

Squamous metaplasia of the urinary bladder is known to occur mainly in women aged more than 50 years, but

also occurs in children and young adult patients.<sup>[16-18]</sup> It may be associated with squamous cell carcinoma. Therefore, the management strategy involves periodic routine cystoscopy for the early detection of transformation from stratified epithelium into neoplastic cells. Some authors have recommended symptomatic treatment for squamous metaplasia of the urinary bladder.<sup>[19,20]</sup> We are continuing to follow up of our patient with cystoscopy and ultrasonography.

Granulomatous cystitis is defined as granulomas in the bladder that occurs because of infections or treatment-related causes.<sup>[21]</sup> In our patient there was no apparent reason.

The most important limitation of this study was the relatively short follow-up period. For practical purposes and brevity in this article, urothelial bladder tumors other than urothelial carcinomas were discussed.

### Conclusion

An important portion of bladder tumors in adolescent and young adults are other than urothelial carcinoma. Unfortunately, although many of these tumors are benign, relapse is not less frequent with these tumors. It is self-evident that these tumors should be closely monitored.

**Conflict of interest:** None

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