Journal of Pediatric Surgery 53 (2018) 306–309

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Urothelial neoplasms in pediatric and young adult patients: A large single-center series☆,☆☆

James A. Saltsman [a], Marcus M. Malek [a], Victor E. Reuter [b], William J. Hammond [a], Enrico Danzer [a], Harry W. Herr [c], Michael P. LaQuaglia [a,*]

[a] Pediatric Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY
[b] Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY
[c] Urology Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY

ARTICLE INFO

Article history:
Received 6 November 2017
Accepted 8 November 2017

Key words:
Urothelial neoplasms
Urothelial carcinoma
Bladder neoplasia
Pediatric
Adolescent

ABSTRACT

Purpose: Bladder cancer is the sixth most common cancer in the United States, but is exceedingly rare in young patients, leading to a lack of accepted standards for diagnosis, treatment, and surveillance. We review our institutional experience with bladder urothelial neoplasms in pediatric and young adult patients summarizing presentation, treatment, and outcomes.

Methods: Surgical pathology records at our institution were searched for cases of urothelial neoplasms among patients ≤25 years of age treated between January 1997 and September 2016. Cases submitted exclusively for pathology review were excluded. Diagnoses were confirmed based on pathologic examination using the 2004 World Health Organization classification system.

Results: Thirty-four patients were identified with a mean age of 21.1 years (range 8–25 years), and median follow-up was 25.1 months (1–187 months). The male to female ratio was 1.83:1. The most common presenting symptom was hematuria (n = 26; 76%). Diagnoses were invasive urothelial carcinoma (n = 3), noninvasive urothelial carcinoma (n = 24), PUNLMP (n = 6), and urothelial papilloma (n = 1). Noninvasive lesions were resected by cystoscopy, after which 12% (n = 4) experienced complications (grade II or greater). One patient with stage IV invasive disease at diagnosis died, and 2 patients developed recurrences. Of those with noninvasive carcinoma, 29% (n = 7) required repeat cystoscopy soon after initial TURBT at outside institutions, and 17% (n = 4) had tumors downgraded from high-grade to low-grade after pathology review.

Conclusion: Hematuria is the most common sign of bladder neoplasia in children and young adults and should be investigated by cystoscopy. The majority of urothelial neoplasms in these patients are noninvasive and can be successfully treated with transurethral resection.

Level of evidence: Level IV (Retrospective study with no comparison group).

Bladder cancer is the sixth most common carcinoma in the United States. An estimated 79,030 new cases will be diagnosed in the United States in 2017 and there will be approximately 16,870 mortalities [1]. Bladder cancer usually occurs later in life, with a median patient age of 73 years at diagnosis; however, a small minority of cases occur in younger individuals, with approximately 0.5% in patients younger than 35 years of age [1]. Previous studies have demonstrated differing findings regarding genetic factors, clinical outcomes, and prognosis of urothelial cancers in young patients [2–8]. These studies are complicated by the fact that there is no established consensus on the definition of young patients, as some restrict analysis to patients younger than the age of 20, while others include patients up to age 45 [4,6]. The definitions and diagnostic criteria of urothelial tumors have also been revised in the time since many of these studies have been published [4,9]. In general, urothelial neoplasms in young patients appear to have distinct genetic, biologic, and clinical features compared to their counterparts in older patients. Urothelial neoplasms in young patients have greater genetic stability [6,7], lower incidence of invasiveness [4,10], and greater overall and disease-free survival compared to adult patients [4,5,8,11,12]. In this study, we review our institutional experience with urothelial neoplasms in patients aged 25 and younger. We present a series of 34 patients, comprising one of the largest single-institution analyses of pediatric and young adult patients with urothelial neoplasms.

☆ Funding: Research at Memorial Sloan Kettering is supported in part by a grant from the National Institutes of Health/National Cancer Institute (#P30 CA008748).
☆☆ Conflict of Interest Disclosure: The authors declare that they have no financial conflicts of interest.
* Corresponding author at: Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY 10065. Tel.: +1 212 639 7002; fax: +1 212 717 3373.
E-mail address: laquaglm@mskcc.org (M.P. LaQuaglia).

https://doi.org/10.1016/j.jpedsurg.2017.11.024
0022-3468/

1. Methods

With institutional review board approval, we reviewed the medical records of 34 consecutive pediatric and young adult patients with urothelial neoplasms who were treated at our institution between January 1997 and September 2016. Inclusion criteria for the study cohort included an age at diagnosis of 25 years or younger and a histologically confirmed diagnosis of urothelial papilloma, papillary urothelial neoplasm of low malignant potential (PUNLMP), or urothelial carcinoma. The definition of these terms is per the 2004 World Health Organization/International Agency for Research on Cancer (WHO/IARC) Classification of Tumors of the Urinary System [13]. According to these guidelines, a urothelial papilloma is defined as a fibrovascular core covered by urothelium indistinguishable from that of the normal urothelium. A PUNLMP is defined as a papillary urothelial tumor that resembles the exophytic urothelial papilloma, but shows increased cellular proliferation exceeding the thickness of normal urothelium. A low-grade noninvasive papillary urothelial carcinoma includes papillary fronds that show an orderly appearance, but demonstrate easily recognizable variations in architecture and cytologic features. A high-grade noninvasive papillary urothelial carcinoma is similar to the low-grade lesion, except it demonstrates a predominant pattern of disorder with moderate-to-marked architectural and cytologic atypia. Finally, an invasive urothelial carcinoma is defined as a urothelial tumor that invades beyond the basement membrane.

Variables reviewed in this study were age at diagnosis, sex, symptoms at presentation, diagnostic methodology, tumor size, histology, surgical treatment, follow-up care, and clinical outcomes. Disease-free survival was calculated using Kaplan–Meier analysis. Statistical analyses were performed with R Statistical Software (version 3.3.3; R Project for Statistical Computing, Vienna, Austria).

2. Results

2.1. Patient and tumor characteristics

A total of 34 patients (65% male, n = 22; 82% Caucasian, n = 28) with a mean age at diagnosis of 20.4 years (range 8–25) and a median follow-up of 25.1 months (range 1–187) were included in the analysis (Table 1). Three patients (9%) in our series were 15 years old or younger at diagnosis. Histologic diagnoses were invasive urothelial carcinoma (n = 3), noninvasive urothelial carcinoma (n = 24; 22 low grade, 2 high grade), PUNLMP (n = 6), and urothelial papilloma (n = 1). The most common symptom at presentation was hematuria, present in 76% (n = 26). Abdominal/pelvic pain was present in 26% (n = 9). Notably, 2 of the 3 patients with invasive lesions presented with abdominal/pelvic pain. Cytology results at time of diagnosis were available for 29 patients. No patients with papilloma or PUNLMP had abnormal cytology, and 3 of 24 patients with noninvasive carcinoma had atypical cells on cytology. Both patients with invasive carcinoma and available cytology had malignant cells present in the urine. The tumor was unifocal in 88% (n = 30) and multifocal in 12% (n = 4). Of the 4 patients with multifocal disease, 2 had invasive carcinoma, one had PUNLMP and one had low-grade non-invasive carcinoma. The location of the tumor was specified in 82% (n = 28) cases and varied significantly; the most common sites were the posterior wall of the bladder (n = 8; 29%), the lateral walls of the bladder (n = 6; 21%), and the trigone (n = 5; 18%). Only one patient had disease in the proximal collecting system. This patient had invasive metastatic disease at diagnosis with a primary lesion in the proximal right ureter. Median tumor size was 0.9 cm for PUNLMP, 2.2 cm for noninvasive carcinoma, and 5.4 cm for invasive carcinoma.

2.2. Treatment

All patients were diagnosed by cystoscopic biopsy, with the exception of one patient with metastatic invasive disease at diagnosis who was diagnosed by CT scan and biopsy. This patient also did not undergo surgery. Of the 33 patients who underwent surgery, complete excision with negative margins was obtained in 91% (n = 30). All three patients with positive margins had low grade noninvasive lesions, and upon repeat transurethral resection of the bladder tumor (TURBT) one of three patients showed no residual carcinoma. Thirty-one resections were performed using TURBT. Both patients with invasive disease who underwent surgery received a laparotomy and partial cystectomy. Three patients with low-grade noninvasive carcinoma received intravesicular chemotherapy at outside institutions: one received mitomycin alone, one received Bacillus Calmette-Guérin (BCG), and one received both drugs. The patient that received both BCG and mitomycin also received treatment with interferon.

2.3. Surveillance

Surveillance cystoscopy was documented in 22 of 33 patients. A median number of five surveillance cystoscopies were performed per patient (range 1–15). The interval between surveillance cystoscopies varied significantly between patients but was generally less than 6 months for the first 1–2 years and 6–12 months thereafter.

Table 1
Patient, disease, and treatment characteristics.

Pathology	Sex	Median age at diagnosis (years)	Urine cytology	Median size in the greatest dimension (no. available)	Treatment	Median follow-up (months)
Urothelial papilloma (n = 1)	1 male	21.4	All negative	1.2 cm (n = 1)	- Transurethral complete excision - No chemotherapy	5.6
PUNLMP (n = 6)	5 males 1 female	19.2	All negative	0.9 cm (n = 5)	- Transurethral complete excision - No chemotherapy	30.5
Low-grade noninvasive urothelial carcinoma (n = 22)	14 males 8 females	21.3	2 (10%) atypical cells	2.2 cm (n = 16)	- Transurethral complete excision - 2 intravesicular mitomycin - 2 intravesicular BCG - 1 interferon	28.3
High-grade noninvasive urothelial carcinoma (n = 2)	1 male 1 female	23.3	1 (50%) atypical cells	Not recorded	- Transurethral complete excision - No chemotherapy	78.8
Invasive carcinoma (n = 3)	1 male 2 females	18.5	2 (100%) malignant cells	5.4 cm (n = 3)	- 2 Laparotomy/partial cystectomy - 1 adjuvant chemotherapy - 1 chemotherapy alone	22.7
All cases (n = 34)	22 males 12 females	21.1	5 (17%) abnormal	2.0 cm (n = 25)	NA	25.1

BCG = Bacillus Calmette-Guerin; NA = not applicable; PUNLMP = papillary urothelial neoplasm of low malignant potential.