



Bladder urothelial neoplasms in pediatric age: Experience at three tertiary centers

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Keywords

Urothelial tumors; Bladder tumors; Children; Painless hematuria; Transurethral resection

Received 21 February 2014
Accepted 11 August 2014
Available online 28 September 2014

Summary

Introduction

Urothelial bladder neoplasms (UBN) typically occur in patients in their sixth or seventh decade of life while they are infrequent in children and young adults. They occur in 0.1–0.4% of the population in the first two decades of life. Their management is controversial and paediatric guidelines are currently unavailable.

Objective

To further expound the available data on the outcome of patients younger than 18 year old diagnosed with UBN.

Study design

We retrospectively reviewed the files of all the consecutive paediatric patients with UBN treated in three tertiary paediatric urology units from January 1999 to July 2013. Lesions were classified according to the 2004 WHO/ISUP criteria as urothelial papillomas (UP), papillary urothelial neoplasm of low malignant potential (PUNLMP), low-grade urothelial carcinoma (LGUC), and high-grade urothelial carcinoma (HGUC).

Results

The table shows the results.

No. of pt		18
Sex	Males	9
Age at diagnosis		11
Mean (range) yr		(3–17)
Presenting symptom	Gross haematuria	16
Workup imaging	Ultrasound (US)	14
	US + CT scan	3
Lesion size		16.7
		(5–50)
Mean (range) mm		
Intravesical location	Lateral wall	4
	Posterior wall	6
	Para-ureteral	8
	Meatus	
Surgical treatment	Trans-urethral resection of bladder (TURB)	18
Additional treatments	Intravesical instillation	1
	Mitomycin-C	
Histology	UP	8
	PUNLMP	8
	LGUC	1
	HGUC	1

Management after TURB varied among centres. One centre recommended only follow-up US at increasing intervals whereas another follow-up US plus urine cytologies and endoscopies, every three months in the first year, and at increasing intervals thereafter. After a median follow-up of 5 years (range 9 months–14.5 years), none of the patients showed disease recurrence or progression.

Discussion

UBN is an uncommon condition in children and adolescents and, unlike in adults, its incidence, follow-up and outcome still controversial. Paediatric guidelines are currently lacking and management varies among centres. Gross painless haematuria is the most common presenting symptom. Therefore, this symptom should never be underestimated. US is generally the first investigation and additional imaging seems unnecessary. TURB often allows for complete resection. Lesions are generally solitary, non-muscle invasive, and low-grade (mainly UP and PUNLMP). Ideal follow-up protocol is the most controversial point. Reportedly, recurrence or progression during follow-up is uncommon in patients under 20 years, recurrence rate 7% and a single case of progression reported so far.

Accordingly, a follow-up mainly based on serial US might be considered in this age group compared to adults where also serial endoscopies and urine cytologies are recommended. In the selection of the follow-up investigations, it should also be taken into consideration that urine cytology has a low sensibility in the detection of low-grade lesions while cystoscopy in young patients requires a general anaesthesia and hospitalization, and carries an increased risk of urethral manipulation.

Conclusion

UBN is a rare condition in children. Ultrasound is generally accurate in order to visualize the lesion, and TURB can treat the condition. Lesions are generally low-grade and non-muscle invasive, but high-grade lesions can also be detected. In present series, after TURB, follow-up US monitoring at increasing intervals was used at all centres, follow-up cystoscopies were added in two centres, but with different schedules. Urine cytologies were considered only at one centre. After a median follow-up of 5 years (range 9 months–14.5 years), none of the patients showed recurrence or progression of the disease.

Introduction

Urothelial bladder neoplasms (UBN) typically occur in patients in their sixth or seventh decade of life, often in relation to a history of smoking or occupational exposure to carcinogenic agents; they are infrequent in children and young adults. Reportedly, they occur in 1–2.4% of the population younger than 40 years, and in 0.1–0.4% of the population in the first two decades of life [1,2].

Given the small number of cases, prognosis of UBN in children is poorly known, and their management is controversial as pediatric guidelines are currently unavailable. One option is to manage these patients by periodical imaging and endoscopic controls, according to common practice in adults [3]. Nevertheless, some authors advocate that UBN in the first two decades of life is a peculiar clinical entity, with a clinical behavior different from the condition seen in adults. They are often solitary, low-grade and non-muscle invasive, and seem to have minimal potential for local recurrence or progression [4]. Accordingly, a less aggressive approach has been advocated [4]. The present study reports the experience with UBN at three tertiary pediatric urology centers, in order to expound the available data on the outcome of these tumors.

Materials and methods

The files of all the consecutive pediatric patients with UBN, treated in three tertiary Italian pediatric urology units from January 1999 to July 2013, were retrospectively reviewed. In all the cases, the diagnosis was confirmed histologically according to the 2004 World Health Organization/International Society of Urological Pathology (2004 WHO/ISUP) criteria [5]. Cases without endoscopic and histological confirmation of the lesion, and those with bladder tumors other than urothelial neoplasm, were excluded. Lesions were classified according to the 2004 WHO/ISUP criteria as: urothelial papillomas (UP), papillary urothelial neoplasm of low malignant potential (PUNLMP), low-grade urothelial carcinoma (LGUC), and high-grade urothelial carcinoma (HGUC) [5].

Data gathered for each study case included gender, age at diagnosis, symptom of presentation, size, location and histology of the lesion, imaging performed for work-up, stage, treatment, follow-up and final outcome in terms of disease progression or recurrence. Given the small sample size, only descriptive statistics were used. Categorical variables were expressed as ratios, and continuous ones as medians (ranges).

Results

A total of 18 patients (nine males), who were followed-up during the study period, were identified. Median age at diagnosis was 11 years (range 3–17), with the age distribution reported in Table 1. The presenting symptom was painless gross hematuria in 16 cases, while in two cases the diagnosis was incidental. The latter included a three-year-old boy, in whom a 12 mm lesion was discovered during a cystoscopy for endoscopic treatment of VUR in a duplex system, and a 12-year-old girl with acanthosis nigricans,

where a 15 mm lesion was discovered during a routine ultrasound (US) in the absence of urinary symptoms.

Urinary tract US was the initial investigation in the 17 patients with a preoperative diagnosis. It showed a solitary bladder lesion with a larger median diameter of 17 mm (range 5–50 mm). In the patient with the incidental diagnosis during endoscopy, the last US had been performed five months before the endoscopy and did not show any evidence of the lesion after retrospective review. This patient was also the only case in the present study with evidence of upper urinary tract dilatation; they had a hydro-ureteronephrosis with an antero-posterior pelvic diameter of 12 mm and a retro-vesical ureter of 7 mm.

All the patients underwent cystoscopy and transurethral resection of the bladder (TURB). Cystoscopy confirmed the presence of a solitary lesion in all of the patients. The tumor was located on the lateral wall of the bladder in four cases, on the posterior wall above the trigone in six, and near the ureteral orifices in the eight remaining patients. The endoscopic resections always appeared to be macroscopically complete. No postoperative complications were observed.

On histological examination, the removed specimen turned up to be a UP in eight cases, a PUNLMP in eight cases, a LGUC in one case and a HGUC in one case. Distribution of the lesions by age is reported in Table 1. None of the lesions had histological evidence of invasion of the underlying tissues, namely: all were non-muscle invasive.

In one center, three patients underwent a Computer Tomography (CT) scan for staging after TURB. The scan showed no evidence of additional lesions. No radiological work-up was performed in the other two centers. One patient with histological diagnosis of PUNLMP received a single intravesical instillation of Mitomycin C after TURB. No intravesical therapy was otherwise used.

Table 2 summarizes the follow-up investigations performed at the three centers. At all centers, US monitoring at increasing intervals was used. Follow-up cystoscopies were used in two centers, but with different schedules. Urine cytologies were considered in one center. After a median follow-up of 5 years (range 9 months–14.5 years), none of the patients showed recurrence or progression of the disease.

Discussion

In this retrospective study of patients with UBN younger than 18 years, all the lesions were solitary and non-muscle invasive, and all but one were low-grade. Transurethral

Table 1 Distribution of tumors by age.

Age range	Number of patients	Histology
<5-years old	1	1 UP
5 to 10-years old	6	1 UP; 4 PUNLMP; 1 LGUC
10 to 15-years old	9	4 UP; 4 PUNLMP; 1 HGUC
>15-years old	2	2 UP

UP: urothelial papilloma; PUNLMP: papillary urothelial neoplasm of low malignant potential; LGUC: low-grade urothelial carcinoma; HGUC: high-grade urothelial carcinoma.

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