Journal of Pediatric Urology (2014) 10, 167—170

Journal of Pediatric urology

Long-term follow-up of transitional cell carcinoma of the bladder in childhood

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Received 14 May 2013; accepted 6 August 2013
Available online 31 August 2013

KEYWORDS
Transitional cell carcinoma;
Tumour;
Bladder;
Childhood

Abstract *Background:* Bladder tumours are rare in children, with only 0.38% of cases occurring in the first two decades of life.
Objective: To describe a long-term follow-up series of nine urothelial bladder tumours in children.
Patients and methods: We carried out a retrospective study covering the period from 1988 until 2005. We found that during this time, urothelial tumours had been diagnosed at our centre in eight patients (9 tumours) younger than 18 years old who reported an episode of haematuria. Diagnosis was attained through renal and bladder ultrasound in 85% of patients, and through cystoscopy under anaesthesia in 15%. All cases were treated by means of transurethral resection of the bladder, with ensuing follow-up using renal and bladder ultrasound and urinary cytology.
Measurements: Patients characteristics and outcome are evaluated.
Results: Single exophytic tumours were present in seven (87.5%) of the patients, located either in the lateral wall or in the trigone; one patient showed two small tumours. The pathology was as follows: two G1Ta, one G1T1, one G2T1, and five G2Ta. There were no recurrences.
Conclusions: Transitional cell carcinoma in childhood is of low grade and low aggressiveness. It has a good prognosis and recurrences are infrequent. We suggest performing a urinary cytology/cystoscopy every 6 months the first 2 years and urinary cytology/bladder ultrasound once a year.

Introduction

Bladder tumours are rare in children, with only 0.38% of cases occurring in the first two decades of life. The origin of such cases is mesodermal. The literature on this topic is very limited, and only small series have been described. In total, some 100 cases of transitional cell carcinoma (TCC) of the bladder in children have been reported since 1950. The tumours have been described as having a low grade of malignancy and showing little tendency to recur. However,

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1477-5131/$36
http://dx.doi.org/10.1016/j.jpurol.2013.08.002

there are no series with a long follow-up of these patients, nor suggestions of how this follow-up should be done. We present our study with transitional bladder tumours and discuss presentation, evaluation, treatment, and especially the long-term follow-up.

Materials and methods

We identified nine urothelial bladder tumours in patients younger than 18 years by means of a retrospective study covering the period from 1986 to 2005. All of the patients attended our centre after an episode of monosymptomatic gross haematuria. It is worth noting that one of the patients, who was 16 years old, was a steady smoker.

Renal and bladder ultrasound were performed in all of the patients, and when the cases were doubtful we also performed cystoscopy under anaesthesia. All patients were treated with transurethral bladder resection, and the bladder catheter was removed 24—48 h after surgery. Slides in each case were classified using the criteria of the WHO 1973. The mean duration of follow-up was 15 years (range 8—27 years), and follow-up was performed by means of renal and bladder ultrasound and urinary cytology every 6 months as well as a cystoscopy once a year for the first 2 years. Afterwards, we performed urinary cytology and bladder ultrasound once a year.

Results

Identifying characteristics of the nine bladder tumours were diagnosed in five males and three females with a mean age of 12 years (range 9—16 years) (Table 1). All of the patients had been investigated at our centre after an episode of monosymptomatic haematuria. Renal and bladder ultrasound identified the lesions in 85% of the patients (Fig. 1), while in 15% diagnosis was achieved by means of cystoscopy under anaesthesia (Figs. 2 and 3). Urinary cytology was negative in all cases.

Transurethral resection (13 Fr resectoscope) of the bladder lesions was performed under general anaesthesia. A single exophytic lesion was identified in seven of the eight patients (87.5%), located either in the lateral wall or in the trigone; one patient showed two small tumours. All lesions measured 0.3—1.3 cm.

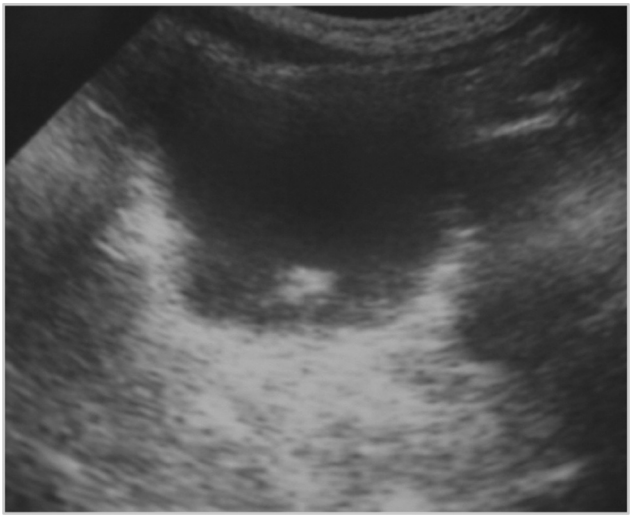

Figure 1 Ultrasound of bladder. A bladder tumour in an 11-year-old boy.

The pathology disclosed was as follows: two G1Ta, one G1T1, one G2T1, and five G2Ta. No recurrence occurred among the TCC cases.

Discussion

Bladder cancer is the third most prevalent carcinoma in humans, accounting for 2.1% of all cancer-related deaths and it has the highest incidence in the sixth decade of life. When diagnosed, 75% of bladder tumours are not muscle invasive. Nevertheless, between 40% and 70% relapse and 20% become invasive in the follow-up. On the other hand urothelial tumours in the first two decades of life are unusual, with most described in case reports and small series in 1969, Javadpour and Mostofi [1] analysed 10,000 patients with urothelial carcinomas, and found only 40 cases in this age group. They described 25 cases in children under 10 years old, and reported a male to female ratio of 3:1 to 9:1. In 2010 Alanee et al. [2] published some descriptive statistics for bladder tumour in children calculated from the Surveillance, Epidemiology and End Results (SEER) database from 1973 to 2003 identifying 15 patients with TCC. Of the

Table 1 Identifying characteristics of eight patients with transitional carcinoma of the bladder who underwent transurethral resection of bladder tumour.

Age (years)	Sex	Symptom	Location	Pathological condition (WHO 1973)	Pathological condition	Recurrence	Diagnosis	Follow-up (years)
9	Male	Haematuria	Trigone	GITa	GITa	No	Ultrasound	20
9	Male	Haematuria	Lateral wall	GIIT1	GII (LGUC) T1	No	Ultrasound	12
10	Male	Haematuria	Lateral wall	GIITa	GII (LGUC)Ta	No	Ultrasound	16
11	Female	Haematuria	Lateral wall	GIITa	GII (LGUC) Ta	No	Ultrasound	13
13	Female	Haematuria	Lateral wall	GIITa	GII (LGUC)Ta	No	Cystoscopy	8
16	Male	Haematuria	Laterall wall Trigone	GIITa GIITa	GII (LGUC) Ta GII (LGUC) Ta	No	Ultrasound	27
15	Male	Haematuria	Lateral wall	G1T1	G1T1	No	Ultrasound	15
16	Male (smoker)	Haematuria	Lateral wall	G1Ta	G1Ta	No	Ultrasound	10

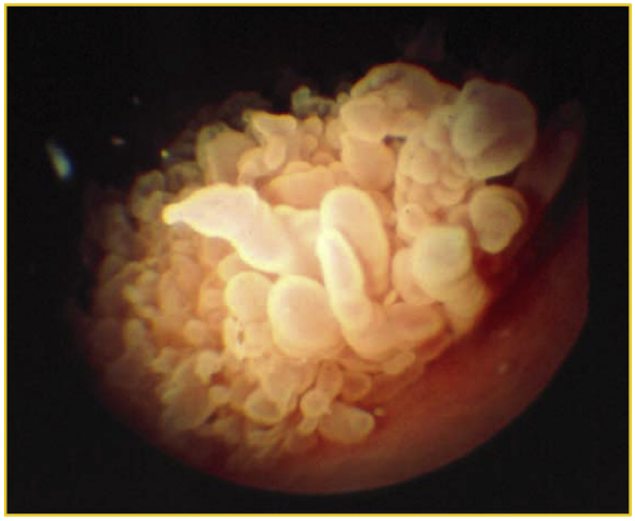

Figure 2 Cystoscopic confirmation of a 1.3-cm papillary tumour in the right lateral wall (AP:G1Ta).

cases, 80% were diagnosed between the ages of 13 and 18 years and only 20% were under 10 years. The survival rate at 5 years was 95% [2].

The risk factors for TCC in adults are well established and include smoking, occupational exposure to aromatic amines, radiation of the pelvis, and cyclophosphamide exposure. Chronic irritation and infection, for example due to *Schistosoma haematobium*, also increase the risk of bladder cancer, particularly squamous cell carcinoma. By contrast, risk factors among the paediatric population are poorly defined: in our series there was one boy with a smoking history, and two other such cases are included in the literature.

In the small series of TCCs of the bladder in children reported in the past, the tumours have typically been described as superficial and low grade (I—II), with a low malignant potential. Owing to the rarity of such cases, however, aetiology, invasive potential, optimal treatment, and survival have not been definitively established [3]. A review of 25 cases by Hoenig et al. [4] disclosed the presence of gross haematuria in 80% of the cases, symptoms of irritation or urinary infections in 15%, and microhaematuria in 5%. The diagnosis was attained by ultrasound in all cases. The selected treatment was transurethral resection of the bladder tumour in 75% of the patients, and open surgery in 25%. Intraoperative findings included single lesions in more than 90% of the cases. The pathology results were as follows: low-grade tumours (I—II) in 100% and only one case of lamina propria invasion (1G2T1). Recurrence occurred in only 2—5% of the patients and was detected by follow-up cystoscopy. Follow-up ranged from 8 to 72 months, without confirming how the follow up was done. Fine et al. [5] published 21 cases of TCC, 18 of which were classified as urothelial neoplasia with a low malignant potential or low-grade carcinomas; only three patients showed high-grade carcinomas. No cases of invasion were seen and 13% recurred with a mean follow-up of 4.5 years.

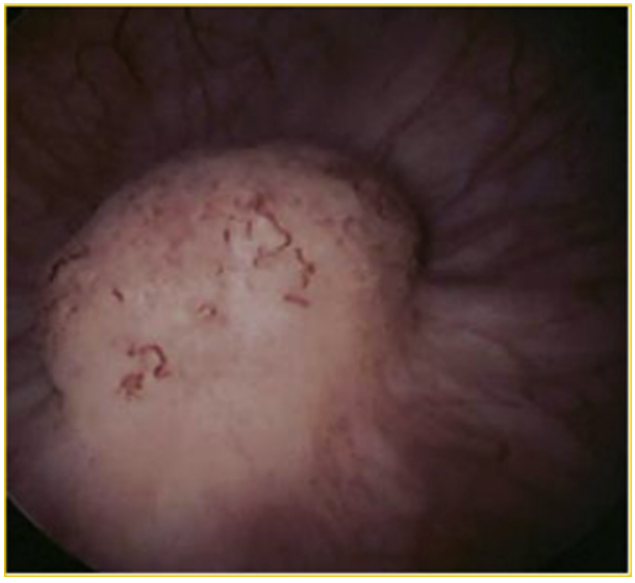

Figure 3 Cystoscopic view of tumoral bladder lesion (AP:G2T1).

All of our patients presented with gross haematuria, a fact that agrees with the 80% rate described in the literature. The sensitivity of ultrasound is high, so it can be performed easily on all paediatric patients suffering from haematuria. In our series ultrasound detected tumours in 85% of the patients; the remaining 15% were diagnosed by cystoscopy under anaesthesia. There were no cases with positive cytology. This finding affirms that the sensitivity of urinary cytology is limited in patients with low-grade TCCs (all 9 in our series were low grade, i.e. grade I or II); however, the sensitivity increases in high-grade tumours (grade III) [6,7].

Lerena et al. published a series of six patients with TCC. All histological studies showing grade I and none of the patients had a recurrence. They state that urinary cytology is a non-invasive method for patient follow-up. However, due to the decrease in sensitivity from 6% to 38% in well-differentiated tumours, endoscopy is required in all cases. As a result, they concluded that urinary cytology is not recommended for diagnosis or follow-up in children [8].

The rarity of recurrence in these tumours in the few published series suggests to us that although TCC of the bladder in this age group may recur, these events are benign or low-grade lesions. Fine et al. [5] described 13% of recurrence, compared with adults with a rate of 40—70%. We believe papillary lesions in young people are not associated with progression to invasive disease. As a result, our recommendation is regular follow-up with renal and bladder ultrasound and urinary cytology because is a non-invasive method for following TCC patients. Cystoscopy enables a final diagnosis but it demands general anaesthesia and is more invasive, so we usually perform a cystoscopy once a year. After a mean follow-up period of 12 years, we observed no case of recurrence of TCC. In view of these good results, we can say that TCC of the bladder is less aggressive in children than in adults. In adults it has a different aetiology and exhibits a different behaviour, with a greater tendency to recur. It should, however, be noted that a study by Paduano and Chiella [9] reported recurrence in two out

of three asymptomatic children, detected by means of a control cystoscopy.

We recommend performing urinary cytology and bladder ultrasound every 6 months as well as a cystoscopy the first 2 years. If there is no recurrence, urinary cytology and a bladder ultrasound will be done once a year.

Conclusions

Urothelial tumours in childhood are infrequent. Our results suggest a good prognosis owing to the low malignancy and the low rate of recurrence. The high sensitivity of ultrasound means that it can be applied in the follow-up of these patients. We assert that renal and bladder ultrasound is the most useful tool for screening children, especially for follow-up in the mid and long term. We suggest carrying out a urinary cytology/cystoscopy every 6 months the first 2 years and urinary cytology/bladder ultrasound once a year.

Conflict of interest

None.

Funding

None.

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