

Papillary Urothelial Neoplasm of Low Malignant Potential in a 9-year-old Boy: A Case Report

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Abstract

Papillary urothelial neoplasm of low malignant potential (PUNLMP) is rarely diagnosed in paediatric patients under the age of 10 years. We report a case of bladder PUNLMP in a 9-year-old boy. The kid presented with painless gross haematuria. Ultrasound and computed tomography imaged a papillary mass in the bladder. Sixteen months follow-up detected no evidence of recurrence after resection of the tumour.

Key words

Bladder; Paediatric; PUNLMP; Urothelial neoplasm

Introduction

Papillary urothelial neoplasm of low malignant potential (PUNLMP) is a new histological diagnosis defined in the WHO 1998 (revised in 2004) / International Society of Urological Pathology (ISUP) classification systems for bladder tumours. According to the definition, PUNLMP is a noninvasive papillary urothelial neoplasm characterised by multilayered urothelium with minimal to absent cytology atypia, and is thought to be a neoplasm with low risk of progression.¹ PUNLMP usually affects adults older than 20 years, and is extremely rare in children younger than 10 years. In the Surveillance, Epidemiology and End Results (SEER) database (1973 to 2003), there are 140 bladder tumours cases of patients younger than 18 years old, and 50.7% of these cases were diagnosed as PUNLMP. Thus,

PUNLMP is regarded as the most common bladder tumour within this age group.² Here, we reported a case of a 9-year-old child with bladder PUNLMP.

Case report

A 9-year-old boy presented with painless intermittent gross haematuria, and without any abdominal mass palpable. An abdominal ultrasound detected an intravesical papillary mass measuring 1.35×1.42 cm (Figure 1A). Computed tomography (CT) indicated that the mass was arising from the right lateral wall of the bladder (Figure 1B). Cystoscopy failed to find the mass due to the defect of rigid cystoscope as well as the mass location, while an intra-operative ultrasound reconfirmed the mass. Cystotomy and resection of the tumour as well as the submucosa and muscular layer was performed.

The pathology reported the bladder PUNLMP, a papillary urothelial neoplasm with branching discrete papillae with fibrovascular core (Figure 2A) which is lined by multilayered urothelium in absence of cytologic atypia (Figure 2B). The cutting edge was negative.

The immunohistochemical staining showed that tumour cells were P53 weak positive, with CK20 negative and Ki-67 proliferative index below 1%. The UroVysion assay reported that chromosome 3, 7, 17 and 9 were normal.

Owing to the benign pathogenic property of PUNLMP

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with purported low incidence of recurrence and progression.³ We have followed up the patient by monitoring progression of the tumour with ultrasound and urinalysis for 16 months. We found that so far there have been no recurrent signs of tumour in the bladder or elsewhere.

Discussion

To our knowledge, this is the first case under the age of 10 years that we reported in China. Our patient is diagnosed with urothelial neoplasm and presented with a typical painless gross haematuria. In one study,¹ 21 out of 23(91.3%) patients 4 to 20 years old with urothelial neoplasm had this common presentation. The main differential diagnoses of bladder neoplasm with painless gross

haematuria include papillary nephrogenic adenoma, fibroepithelial polyp, urothelial papilloma, urothelial carcinoma, haemangioma, rhabdomyosarcoma, inflammatory fibroid tumour, and paraganglioma. Overall, the management of these bladder neoplasms are usually followed by pathological examination. Delay in diagnosis of urothelial neoplasm in young patient, particularly in those younger than 20 years, is not uncommon because of the low clinical index of suspicion and lower inclination to perform cystoscopy that requires general anaesthesia in younger patients and has the risks of urethral manipulation. Essentially, ultrasound monitoring is an extremely sensitive and effective approach in identifying bladder urothelial lesions in paediatric patients. In this case, pre- and intra-operative ultrasound identified the tumour rather than rigid cystoscopy. Theoretically, flexible cystoscopy provide



Figure 1 (A) An ultrasound image showed an intravesical papillary mass (arrow) with size of 1.35x1.42 cm; (B) The CT image revealed the mass (arrow) arising from the right lateral wall of the bladder.

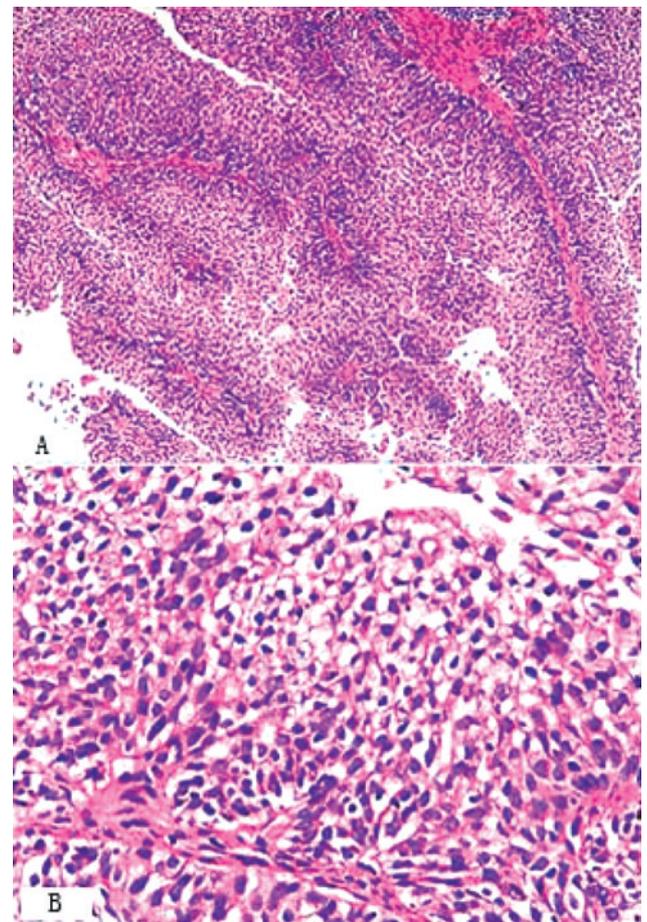


Figure 2 (A) Low-power (x50) view of the papillary neoplasm; (B) High-power (x200) view of the increased thickness of epithelium in the absence of cytologic atypia.

better view to identify lesions in comparison with rigid cystoscopy, such as in the lateral wall, flexible one was not available in our hospital until six months ago. CT especially contrast-enhanced ones can represent the accurate imaging modality for the detection of bladder tumour as well as magnetic resonance imaging. However, the risk of radiation exposure and allergic reaction to contrast material has to be balanced against the disease likelihood in young patients. We chose ultrasound and unenhanced CT for this child as he had history of allergy to contrast material.

PUNLMP in children may differ from that in adults in its biological behaviour and most likely in its aetiology. Cigarette smoking is a known contributing factor for bladder urothelial carcinoma, but the impact of smoking is considered likely to be minimal to absent in patients younger than 20 years compared with the older patients.⁴ Bladder urothelial carcinoma is associated with several occupational exposures in older patients. However, there is no definitive evidence linking occupational exposure to bladder tumour in young patients.⁴ This child neither had history of smoking or family member who smoked, nor accompanied with exposure to carcinogens. Overall, there are evidence for possible genetic link for PUNLMP in young patient.⁵ However, overlap with environment risk factors makes it difficult to provide a definitive conclusion. Further epidemiological studies and genetic research concerning the aetiology of PUNLMP in paediatric cohort should be performed.

Because of the reported variable increased incidence rates of recurrence (10% to 45%) and progression (0 to 29%)^{1,2,3,6} after resection of PUNLMP, patients are subsequently monitored for recurrence and/or progression by regular cystoscopy necessitating anaesthesia in most paediatric patients. Some argue against invasive cystoscopy for the risk of urethral damage and the necessity for anaesthesia. Noninvasive modality like ultrasound, urinalysis and cytology are recommended as surveillance protocol. In this case, we preferred to select ultrasound and urinalysis for detecting any recurrence once a month. But there is no defined protocol for how often and how long these young patients need to be followed up.

Recently, molecular and immunohistochemical adjuncts were considered helpful for diagnosis and predicting recurrence and progression. Yin and Leong⁷ found that Negative P53, normal CK2 to be seen in PUNLMP cases which were predictive of low recurrence and progression. And these biologic markers can provide additional objective criteria for the grading of papillary urothelial tumours. This child had a similar

immunohistochemical staining report above predicting a good outcome.

In summary, PUNLMP is rare in children and seems to have excellent long-term outcome. Use of PUNLMP diagnosis in younger patients provides strong support for the creation of this entity, which avoids "cancer" diagnosis in the very young patients with bladder urothelial neoplasm who will have a favourable outcome. There are no established criteria for the diagnosis, treatment and surveillance for PUNLMP in the young or paediatric population. For early diagnosis of PUNLMP, children presenting with gross haematuria should be carefully evaluated. Minimally invasive diagnostic modalities should be preferentially used for surveillance. Ultrasound is extremely effective in identifying bladder urothelial lesions. And thus, we strongly recommend it for early diagnosis and surveillance in paediatric patients with PUNLMP.

Declaration of Interest

We declare that we have no conflict of interests.

References

1. Fine SW, Humphrey PA, Dehner LP, Amin MB, Epstein JI. Urothelial neoplasms in patients 20 years or younger: a clinicopathological analysis using the world health organization 2004 bladder consensus classification. *J Urol* 2005;174:1976-80.
2. Alanee S, Shukla AR. Bladder malignancies in children aged <18 years: results from the surveillance, epidemiology and end results database. *BJU Int* 2010;106:557-60.
3. Jones TD, Cheng L. Papillary urothelial neoplasm of low malignant potential: evolving terminology and concepts. *J Urol* 2006;175:1995-2003.
4. Paner GP, Zehnder P, Amin AM, Husain AN, Desai MM. Urothelial neoplasms of the urinary bladder occurring in young adult and pediatric patients: a comprehensive review of literature with implications for patient management. *Adv Anat Pathol* 2011; 18:79-89.
5. Mueller CM, Caporaso N, Greene MH. Familial and genetic risk of transitional cell carcinoma of the urinary tract. *Urol Oncol* 2008;26:451-64.
6. Lee TK, Chau A, Karram S, et al. Papillary urothelial neoplasm of low malignant potential of the urinary bladder: clinicopathologic and outcome analysis from a single academic center. *Hum Pathol* 2011;42:1799-803.
7. Yin H, Leong AS. Histologic grading of noninvasive papillary urothelial tumors: validation of the 1998 WHO/ISUP system by immunophenotyping and follow-up. *Am J Clin Pathol* 2004;121: 679-87.