CASE REPORT

Urothelial papilloma: a rare cause of gross haematuria in childhood

Andreia Ribeiro,¹ Maria Pereira,¹ Armando Reis,² Graça Ferreira¹

¹Department of Paediatrics, Hospital Center of Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal

²Department of Paediatric Urology, Oporto Hospital Center, Oporto, Portugal

Correspondence to

Dr Andreia Ribeiro,
andrea.ribeiro@chvng.min-saude.pt

Accepted 1 May 2017

SUMMARY

Bladder urothelial papilloma is extremely rare in the paediatric population. It usually presents as painless gross haematuria and its diagnosis implies a high index of suspicion as other causes of haematuria predominate in this age range. We describe a 9-year-old boy with two episodes of gross haematuria occurring 1 year apart with spontaneous resolution after 2 days. Bladder ultrasound revealed an endovesical papillary lesion of 24×24 mm suggestive of bladder tumour. The diagnosis was confirmed by histopathological examination of the specimen obtained by cystoscopy with transurethral resection. After 3 years of follow-up with ultrasound and cystoscopy, there are no signs of recurrence. Due to the low prevalence of urothelial papilloma, paediatric guidelines for appropriate management and follow-up are unavailable, making this a challenging entity.

BACKGROUND

Gross haematuria is unusual in childhood and is frequently a matter of anxiety to the child and family. The most common causes of gross haematuria in children are urinary tract infection (UTI), trauma and urethral meatus irritation.¹ Most frequently the cause is easily recognisable after a complete initial evaluation which includes a detailed history, physical examination and urinalysis.

Urothelial bladder neoplasms (UBNs) are a rare cause of gross haematuria. They typically occur in the sixth or seventh decade of life and are extremely rare in children,² with fewer than 30 cases reported under those aged 10 years³ and an estimated prevalence of 0.1%–0.4% in the first two decades of life.^{2,4}

Urothelial papillomas (UPs) are an exophytic non-invasive urothelial neoplasm composed of a delicate fibrovascular core covered by urothelium of normal thickness and normal-appearing cytology, as defined by the 2016 WHO classification.^{5,6} They account for only 1%–4% of all bladder tumours.⁷ The designation ‘papilloma’ has been used differently by diverse authors as a result of classification continuous update, in such a way that it is still in discussion if UP can be considered a benign lesion. This, associated with their low prevalence in paediatric population, makes appropriate management and prognosis poorly known.

CASE PRESENTATION

A previously healthy 9-year-old boy was referred to paediatric nephrology department after two

episodes of painless gross haematuria occurring 1 year apart with spontaneous resolution. Urinalysis and renal ultrasound performed at the first episode were normal. Microhematuria was detected by urinalysis between episodes after physical exercise but normalised thereafter. At the second episode, the child reported a 2-day history of haematuria and dysuria. There was no history of trauma, fever or other complaints.

His father worked with varnish, glue and diluent and the child had frequent visits to his office. Family history was positive for a single episode of gross haematuria in a second-grade cousin.

Detailed physical examination was unremarkable. Renal and bladder ultrasound described echogenic material in the bladder suggestive of blood clots with no other relevant findings, although the bladder was empty precluding a more accurate assessment. Urinalysis confirmed haematuria (250 erythrocytes/ μ L) with no other alterations and urine culture was negative. Complete blood cell count, electrolyte levels, liver function tests, creatinine, urea nitrogen, protein, immunoglobulins, C3 and C4, anti-streptolysin O, antinuclear antibody, antineutrophil cytoplasmic antibody, C reactive protein, prothrombin and partial-thromboplastin time were within normal ranges.

Urinalyses of all other family members were normal. Repeated urinalysis normalised thereafter with normal urinary calcium/creatinine ratio. Bladder ultrasound was repeated which revealed an endovesical papillary lesion of 24×24 mm located on the left side of the bladder floor with a Doppler-detected flow suggestive of bladder tumour (figure 1).

A cystoscopy with transurethral resection of bladder tumour (TUR-BT) was performed with apparent excision of the entire lesion. The postoperative course was uneventful. Histopathological examination of the specimen revealed an epithelial proliferative lesion with papillary architecture consistent with UP according to the 2016 WHO classification (figure 2).⁶ There was no evidence of invasion of underlying tissues.

OUTCOME AND FOLLOW-UP

Follow-up ultrasound monitoring was negative and a cystoscopy carried out 6 months after surgery was normal. After 3 years of follow-up, the patient remains asymptomatic and with no signs of recurrence or progression.

CrossMark

To cite: Ribeiro A, Pereira M, Reis A, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-219341

Figure 1 Bladder ultrasound. A solitary polypoid lesion of 24×24 mm is visible in the bladder.

DISCUSSION

In the paediatric population, UBNs are more frequent in the late years of adolescence (67.0% at 15–20 years of age vs 13.6% under 10 years of age) and have a male predominance, including when exclusively UPs are evaluated.⁸ In a retrospective study, eight cases of UP were diagnosed over a 14-year period in three paediatric urology units,² with others presenting only two cases of UP over a 12-year period.⁷

Well-documented environmental risk factors for UBN in adults may play a minor role among paediatric cohort as the latency period required after exposure is fairly long. For example, cigarette smoking and aromatic amine usually found in paint, rubber, dyes and diesel exhaust are well-known risk factors for bladder urothelial carcinoma in adults; however, the same association is not proven in young patients with UBN.^{3,8} The exposure to aromatic amines in our case is therefore probably a coincidence and further research is required.

UBNs have a broad spectrum of presenting symptoms with gross haematuria being the most frequent (90%), as described in this case.^{3,8} Other less frequently reported manifestations are

irritative voiding symptoms (dysuria, frequency and urgency), urinary tract obstruction, abdominal pain, fever, nephrolithiasis and emesis.³

The differential diagnosis of painless gross haematuria in the paediatric age is vast and entities other than UBN predominate, with UTI being the most frequent one. Only 0.9% of patients under 20 years of age with gross haematuria are eventually diagnosed with UBN.^{3,9} Usually, additional investigations are only executed if the symptom persists and in up to one-fourth of patients there is at least 1 year of delay from initial presentation to diagnosis.^{2,4,8,10} In this case, although the first episode of haematuria was unlikely related to the UBN, bladder ultrasound was not performed, making it impossible to ascertain. At the second episode, the symptom persistence and negative urine culture pointed towards another entity justifying a more extensive investigation. Therefore, the diagnosis of UBN requires a high index of suspicion and bladder ultrasound should be performed in every case of haematuria not related to UTI or trauma² and in cases of recurrent or persistent haematuria.⁴

Bladder ultrasound should be used as first clinical approach to identify UBN, given its good specificity and high sensitivity with the ability to detect lesions as small as 5 mm.² However, full bladder is necessary to avoid false negative results as occurred in the first bladder ultrasound of this patient. Despite being considered the gold standard for diagnosis, cystoscopy is a more invasive exam that requires general anaesthesia in young patients. It should therefore be reserved to obtain a specimen for histological examination and final diagnosis of a lesion detected by ultrasound. Urine cytology has a minimal role in UBN diagnosis despite its high specificity (98%), because of its low sensitivity (34%) especially to low-grade lesions (12% for grade 1 tumour).¹¹

Clinical behaviour of UBN (including UP) is controversial among different authors, with the majority of studies reporting a more favourable prognosis with a predominance of low-grade and superficial-stage tumours in younger patients compared with adults.^{8–10} Metastatic disease and aggressive UBN are rare under 20 years of age, with a low rate of recurrence (3.4%), progression (1.1%) and death (1.1%).^{8,12} Nevertheless, studies reveal that low-grade non-muscle invasive UBN, including UP, can recur⁸; recurrences can be multiple and can occur many years after the initial diagnosis occasionally with progression to higher-grade disease.^{2,8}

Recommendations for management and surveillance of UBN in children are not completely established given its unique aetiological, pathological and clinical characteristics.⁸ Initial management with TUR-BT is consensual with no other therapy preconised for UP. Although not any more recommended in the majority of paediatric studies, postoperative intravesical chemotherapy is still done for higher-grade tumour in some units, according to adults guidelines.^{2,10}

Long-term disease surveillance varies widely among authors. Although time of follow-up should be proportional to the risk of disease recurrence and progression, there are still conflicting data on the natural history of UBN in children.² Few studies propose that the clinical course of UBN is comparable to the adults and requires an aggressive follow-up^{9,13}; others suggest a less aggressive approach as it might have a benign clinical behaviour.^{2,10,14}

Ultrasound has proven to be highly efficient for surveillance of UBN comparatively with cystoscopy and urine cytology.^{10,15} CT should not be used for this purpose given its lower sensitivity compared with ultrasound.³ Programme of surveillance varies among authors with some suggesting a 2-year follow-up with

Figure 2 Histological examination of urothelial papilloma. (A) Epithelial proliferative lesion with papillary fronds. (B) Fibrovascular core of papilloma covered by normal thickness urothelium and prominent superficial umbrella cells.

cystoscopy every 6 months⁷ while others propose clinical examination and ultrasound carrying out at 3, 6, 12 months and then annually.¹⁶ In this case, cystoscopy was executed 6 months after TUR-BT to confirm complete resection and consecutive follow-up was carried with bladder ultrasound every 6 months. Owing to the usual benign behaviour of UP, we consider a conservative approach suitable, with ultrasound having adequate sensitivity for the diagnosis and follow-up.

Duration of follow-up is not consensual in the literature, although long-term follow-up seems reasonable in young patients to help determine its prognostic significance and potential biological course.¹²

Learning points

- Urothelial bladder neoplasms are a rare condition in the paediatric age but should be considered in every case of gross haematuria since that is its most frequent form of presentation.
- Initial investigation should include ultrasound followed by cystoscopy with transurethral resection to confirm and remove the tumour.
- Although low-grade and low-stage disease is more frequent in children, recurrences have been described reinforcing the importance of long-term follow-up.
- As paediatric guidelines for appropriate management and follow-up are lacking, long-term studies are required.

Contributors All authors have contributed for this work. The article has been read and approved by all authors. Specifically, AR has contributed to literature research, acquisition and data analysis, conception and writing the article. MP has contributed to literature research, acquisition and data analysis, and drafting the article. GF and AR have participated in conception, writing and revision of the article for important scientific content.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Patel HP, Bissler JJ. Hematuria in children. *Pediatr Clin North Am* 2001;48:1519–37.
- 2 Berrettini A, Castagnetti M, Salerno A, et al. Bladder urothelial neoplasms in pediatric age: experience at three tertiary centers. *J Pediatr Urol* 2015;11:26.e1–26.e5.
- 3 Chu S, Singer J. Transitional cell carcinoma in the Pediatric patient: a review of the Literature. *Urology* 2016;91:175–9.
- 4 Ander H, Dönmez Mİ, Yitgin Y, et al. Urothelial carcinoma of the urinary bladder in pediatric patients: a long-term follow-up. *Int Urol Nephrol* 2015;47:771–4.
- 5 Humphrey PA, Moch H, Cubilla AL, et al. The 2016 WHO classification of Tumours of the Urinary System and Male Genital Organs-Part B: prostate and bladder tumours. *Eur Urol* 2016;70:106–19.
- 6 Moch H, Humphrey PA, Ulbright TM, et al. *WHO classification of Tumours of the Urinary System and Male Genital Organs*. Lyon, France: International Agency for Research on Cancer, 2016.
- 7 Apoznański W, Rysiakiewicz J, Polok M, et al. Transurethral resection of the bladder tumour as a treatment method in children with transitional cell carcinoma of the bladder—analysis of our Material and Literature Review. *Adv Clin Exp Med* 2015;24:505–9.
- 8 Paner GP, Zehnder P, Amin AM, et al. 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;18:79–88.
- 9 Migaldi M, Rossi G, Maiorana A, et al. Superficial papillary urothelial carcinomas in young and elderly patients: a comparative study. *BJU Int* 2004;94:311–6.
- 10 Polat H, Utangac MM, Gulpinar MT, et al. Urothelial neoplasm of the bladder in childhood and adolescence: a rare disease. *Int Braz J Urol* 2016;42:242–6.
- 11 Lotan Y, Roehrborn CG. Sensitivity and specificity of commonly available bladder tumor markers versus cytology: results of a comprehensive literature review and meta-analyses. *Urology* 2003;61:109–18.
- 12 El Rahman DA, Salvo G, Palumbo C, et al. Bladder tumours in children: an interesting case report of TCC with a partial inverted growth pattern. *Arch Ital Urol Androl* 2014;86:222–3.
- 13 Yossepowitch O, Dalbagni G. Transitional cell carcinoma of the bladder in young adults: presentation, natural history and outcome. *J Urol* 2002;168:61–6.
- 14 Al Bashir S, Yilmaz A, Gotto G, et al. Long term outcome of primary urothelial papilloma: a single institution cohort. *Pathology* 2014;46:37–40.
- 15 Fine SW, Humphrey PA, Dehner LP, et al. 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.
- 16 Umlauf VN, Coerd W, Leuschner I, et al. How to name papillary tumors of the bladder in Children: transitional cell carcinoma or papillary urothelial neoplasm of low malignant potential? *Urology* 2015;86:379–83.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow