

# Repeated endoscopic treatments of multiple recurrent ureteral tumors following 15-year-long history of bladder tumors in the patient from endemic nephropathy region

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Ureteral urothelial tumors (UUT) are uncommon; their incidence is higher in areas affected by Balkan endemic nephropathy (BEN), with low-grade lesions prevalent. In these patients, the efficacy of conservative surgery is comparable to that of nephroureterectomy. Endoscopic treatment is indicated for single, small and low grade UUT, in older patients with significant comorbidity.

The case of an 84-year-old lady from an area affected by BEN is presented. Over 20 years, the patient underwent five endoscopic interventions for multiple UUT, and numerous endoscopic interventions for recurrent bladder tumors.

Among a highly select group of patients, endoscopic treatment of multiple small superficial low-grade ureteral tumors may prove successful.

**Key Words:** bladder tumors ◊ endoscopic management ◊ ureteral tumors

## INTRODUCTION

In contrast to bladder tumors (BT), ureteral urothelial tumors (UUT) are uncommon; the BT: UUT ratio is 33:1 [1]. The incidence of UUT is higher in areas affected by Balkan endemic nephropathy (BEN), with low-grade lesions prevalent [2].

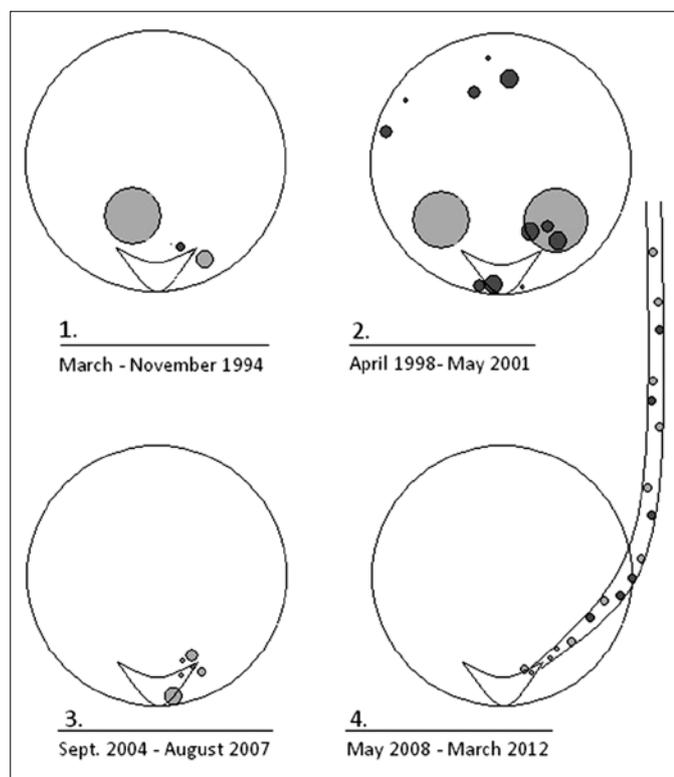
All urothelial tumors have a propensity for multicentric growth in space and time and a high rate of recurrence; almost every second BT will recur [3]. Patients with UUT face a BT development risk of 20–50%, while the risk is 10 times lower inversely.

The standard treatment for UUT is total nephroureterectomy (NU). However, it has been proved that the efficacy of conservative surgery is comparable to that of NU in patients from areas affected by BEN [4].

Endoscopic treatment is indicated for single, small (<1.5 cm) low-grade tumors in older patients at risk from open radical surgery, a solitary kidney, or bilateral disease [5]. If there is a recurrence, it can be treated with an additional endoscopic procedure.

## CASE REPORT

The case of an elderly lady from the area affected by BEN is presented. The lady was born in 1929 in a small village in south eastern Serbia; she has never smoked. In March 1994 she underwent her first transurethral resection (TUR) of a bladder tumor. A pathological examination revealed transitional cell cancer (TCC) stage Ta, grade G1. Over the next 20 years the woman had 24 recurrent low-grade BTs and five ureteroscopic fulgurations for about 30 urothelial tumors in the left ureter (Figure 1).



**Figure 1.** The positions and size of the tumors in the urinary bladder and left ureter from March 1994 – March 2012.



**Figure 2.** Intravenous urography presenting multiple tumors in the lower part of the left ureter (April 2009).

The first ureteral tumor was seen during a routine cystoscopy, emerging from the left orifice. The tumor was biopsied and fulgurated: pathological examination revealed ureteral TCC, minimal TaG1. All further recurrent ureteral tumors were TaG1; they were discovered by URS after two and after five months and fulgurated immediately. Ten months after the appearance of the first ureteral tumor, intravenous urography (IVU) revealed the presence of multiple defects in the left ureter suggestive of tumors (Figure 2).

Subsequently, URS confirmed the presence of at least five tumors in the upper ureter and at least 10 tumors in the lower ureter. The tumors in the lower ureter were biopsied, while all other tumors were fulgurated without biopsy. The next evidence of recurrence was in the left ureter after 10 months (one tumor) and after 20 months (10 tumors) (Figure 3).

Once again, tumors were treated by means of URS and fulguration. Six months later, no recurrence was evident. Ten months later, three 3–5 mm large tumors had occurred in the bladder, around the left orifice. Today, the patient is 84 years old and shows no signs of the disease.

## DISCUSSION

The author finds this case interesting for a number of reasons: primarily due to the long history of bladder tumors without progression. Furthermore, the history of the disease can be divided into two parts: in the first 10 years malignant transformation took place in various parts of the bladder; in later years the left ureter was the source of malignant cells. The appearance of multiple small BTs around the left orifice was most probably the result of downstream seeding of malignant cells from the ureter. In addition, the ureteral tumors were small and low grade, without progression, which is not typical [6]. Finally, five years after the first URS–fulguration, despite multiple recurrences and repeated procedures, the patient is quite well and disease-free.

Intravesical BCG therapy was administered twice, in 1994 and 1998; the duration of the therapy was

36 months. After 2001, there was a recurrence-free interval, followed by a period of small low-grade intraurethelial neoplasias, so BCG therapy was not continued. Intraurethelial BCG therapy is generally recommended after conservative treatment of UUT, especially where carcinoma is present *in situ* [7] by percutaneous nephrostomy (PCN), or through a ureteric stent. However, the long-term results have not been confirmed. In this case, the patient did not receive intraurethelial BCG: the tumors were low-grade, so there was no need for PCN. A Double-J catheter was inserted to prevent ureteral stenosis. Nevertheless, the fact that massive recurrence appeared nine months later is convincing evidence that topical BCG was actually indicated.

As the patient was reluctant to accept NU, conservative treatment was considered. However, indications did not quite accord with EAU guidelines (unifocal tumor), rather the tumors were small, non-infiltrative and low grade [6]. In addition, the patient was elderly and came from an area affected by BEN. Given the lack of laser equipment, which is in all likelihood superior [8], URS with fulguration was performed.

In the period 2001–2004, the follow-up consisted of control cystoscopy and urine cytology every six months, with a three-month interval between cystoscopy and urine cytology. Subsequently, due to frequent recurrences, control cystoscopy was performed every three months. After the first URS-fulguration, diagnostic URS was performed every three months. More recently, URS has been repeated every 3–5 months, in combination with 3D reconstruction-CT urography. Although it is recommended, especially in muscle-invasive disease [9], ureteral cytology has not been performed, due to frequent URS.

It is interesting that despite the patient having 24 BTs and over 30 UUTs this does not reflect the extent of the disease. Specifically, if tumor volume is calculated using the sphere formula, the total volume of all BTs is around 60 mL, yet the total volume of all UUTs is only 1.1 ml. This fact also justifies the “ureter-sparing” procedure, despite the large number of tumors.



**Figure 3.** The three-dimensional (3D) reconstruction based on CT-urography showing at least 10 recurrent tumors in the left ureter (February 2012).

The only complications were three stenoses in the left ureter, which were mild and did not progress. Endoscopic treatment of UUT should not always be limited to single ureteral tumors. It can be successfully performed in a highly select group of elderly patients with multiple small superficial low-grade UUT, especially if they originate from areas known for a low UUT malignancy potential. These patients require strict follow-up.

## References

1. Sagalowsky AI, Jarrett TW, Flanigan RC: Urothelial Tumors of the Upper Urinary Tract and Ureter. In Campbell-Walsh Urology, 10th ed. Editor-in-chief: Alan J. Wein. Editors: Louis R. Kavoussi, Alan W. Partin, Craig A. Peters and Andrew C. Novick eds, Philadelphia: Saunders; 2012, Chapt 53, pp. 1517–1553.
2. Nikolic J, Djokic M, Ignjatovic I, Stefanovic V. Upper urothelial tumors in emigrants from Balkan endemic nephropathy areas in Serbia. *Urol Int.* 2006; 77: 240–244.
3. Montironi R, Lopez-Beltran A. The 2004 WHO classification of bladder tumors: a summary and commentary. *Int J Surg Pathol.* 2005; 13: 143–153.
4. Petković S, Mutavdžić M. The late results of conservative surgery for ureteral tumours. *Br J Urol.* 1968; 40: 412–414.
5. Gadzinski AJ, Roberts WW, Faerber GJ, Wolf S Jr. Long-term outcomes of nephroureterectomy versus endoscopic management for upper tract urothelial carcinoma. *J Urol.* 2010; 183: 2148–2153.
6. Rouprêt M, Zigeuner R, Palou J, Boehle A, Kaasinen E, Sylvester R, et al. European

- guidelines for the diagnosis and management of upper urinary tract urothelial cell carcinomas: 2011 update. *Eur Urol.* 2011; 59: 584–594.
7. Thalmann GN, Markwalder R, Walter B, Studer UE. Long-term experience with bacillus Calmette–Guerin therapy of upper urinary tract transitional cell carcinoma in patients not eligible for surgery. *J Urol.* 2002; 168: 1381–1385.
8. Hubosky SG, Boman BM, Charles S, Bibbo M, Bagley DH. Ureteroscopic management of upper tract urothelial carcinoma (UTUC) in patients with Lynch Syndrome (hereditary nonpolyposis colorectal cancer syndrome). *BJU Int.* 2013; doi: 10.1111/bju.12008 [Epub ahead of print]
9. Brien JC, Shariat SF, Herman MP, Ng CK, Scherr DS, Scoll B, et al. Preoperative hydronephrosis, ureteroscopic biopsy grade and urinary cytology can improve prediction of advanced upper tract urothelial carcinoma. *J Urol.* 2010; 184: 69–73. ■