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Upper Urinary Tract Urothelial Carcinomas: Benefits of Diagnostic Ureteroscopy and Results of Conservative Treatment

Mohammed Benamar[1*], Vincent Richard[2], Mustapha Ahsaini[1], Soufiane Mellas[1], Jalal Eddine El Ammari[1], Mohamed Fadl Tazi[1], Mohammed Jamal El Fassi[1], Moulay Hassan Farih[1]

[1]Urology Department, Hassan II University Hospital, Fez, Morocco
[2]Urological Surgery Department, Hôpital Nord Franche Comte, Trevenans, France

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***Corresponding author:** Mohammed Benamar
Urology Department, Hassan II University Hospital, Fez, Morocco

Abstract | **Case Report**

Upper urinary tract urothelial carcinomas (UTUC) are rare and predominantly male. They may be multifocal in around 30% of cases. They are of particular interest because of the difficulties involved in their diagnosis. We report a series of 08 patients collected in the urology department of the Hôpital Nord Franche-Comte (HNFC) in Trevenans between 01/2019 and 03/2022. There were 05 men (62.5%) and 03 women (37.5%) with an average age of 70.85 years. Clinical symptoms were dominated by low back pain in 04 patients (50%), haematuria in 2 patients (25%), and a combination of low back pain and haematuria in 1 patient (12.5%). The finding was fortuitous in 1 patient (12.5%). The uroscanner performed in all our Patients revealed ureteral lesions in 7 patients (87.5%), a combination of ureteral lesion and ureteropyelocalic dilatation (UPD) in 4 patients (50%) and a normal uroscanner in 1 patient (12.5%). Ultrasound was not performed in any of our patients. Cystoscopy revealed an infracentimetric polyp at the level of the bladder dome in 3 patients (37%), including 1 patient undergoing surveillance for UTUC and who had no history of bladder tumour; the other 2 were already being monitored for bladder tumour; a trigonal polyp measuring approximately 3cm in 1 patient (12.5%) who had a history of bladder tumour, an infracentimetric floor polyp in 1 patient (12.5%) who had no history of bladder tumour, and normal cystoscopy in the other 3 (37.5%). Ureteroscopy revealed a papillary lesion measuring approximately 1cm in the middle calyx of the right kidney in 1 patient (12.5%), a lesion of the pelvic ureter in 4 patients (50%) measuring approximately 1.5cm, 2cm, 3cm in the first 3 patients and a lesion occupying the entire pelvic ureter in the 4th patient; a lesion of the iliac ureter in 3 patients (37.5%) whose sizes are approximately 1cm, 2cm, and 4cm. Urine cytology showed a strong suspicion of a high-grade urothelial lesion in 2 patients (25%), an appearance of a low-grade urothelial lesion in 3 patients (37.5%) and an uncertain malignancy potential in 3 patients (37%). Anatomical Pathology was consistent with low grade (LG) Pta urothelial carcinoma in 6 patients (75%), probable LG tumour in 1 patient (12.5%) and LG Pt1a urothelial carcinoma in 1 patient (12.5%). Thoracic, abdominal and pelvic (TAP) CT-scan did not show any secondary locations in any of our patients. All our patients had undergone laser photovaporisation. Follow-up was marked by recurrence of UTUC at 3 months in 1 patient (12.5%), recurrence of UTUC at 3 months, 9 months, 1 year and 2 years in 1 patient (12.5%); recurrence of ureteral and bladder tumours at 1 year in 1 patient (12.5%), recurrence of UTUC tumour after 9 months in 1 patient (12.5%), appearance of a bladder tumour after 1 year without recurrence of the UTUC in 2 patients (25%) who had no history of bladder tumour, and absence of recurrence after 1 year control in 2 patients (25%). On the basis of these observations and several reviews of the literature, we analysed the epidemiological and pathological aspects and the results of conservative treatment of upper urinary tract urothelial carcinomas.

Keywords: Upper urinary tract-Urothelial carcinoma-Laser photovaporisation.

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INTRODUCTION

Upper urianary tract urothelial carcinomas (UTUC) are tumours represented mainly by urothelial carcinoma and develop in the pyelocalic cavities or the ureter. These tumours are rare (around 1 case/100,000/year), the average age at diagnosis is late (around 70), and they affect more men than women (1.5 to 2.5 to 1). The way in which they are discovered varies, either fortuitously in the context of research or follow-up of another pathology such as bladder tumour, bearing in mind that 2 to 4% of patients with a bladder tumour develop a tumour of the upper urinary tract synchronously or metachronously, or in the presence of

clinical signs that may be variable such as haematuria or low back pain [1].

Total nephro-ureterectomy with excision of a perimeter bladder flange remains the standard treatment for localised lesions, but conservative endoscopic treatment using laser photovaporisation or segmental resection may be considered in a few well-defined indications. At present, several studies are investigating UTUC, particularly new treatment options, to broaden the therapeutic arsenal [19].

Aim of the study: To assess the value of ureteroscopy in the diagnosis of UTUC and its role in conservative treatment.

MATERIAL AND METHOD

This is a single-centre retrospective study, over a period of 3 years between 01/2019 and 03/2022, targeting a population of 08 patients, collected in the urology department of the Hôpital Nord Franche-comte in Trevenans.

The data were collected using a computerised system set up at the Nord Franche-Comte Hospital, with codes for diagnostic ureterorenoscopy: JCNE004, JCNE002 and JCNE003.

Inclusion criteria:

All patients with UTUC who had undergone endoscopic treatment by photovaporisation.

Exclusion criteria:

All patients with UTUC who had undergone initial surgical treatment by either segmental ureterectomy or total nephroureterectomy.

***Limitations of our study*:**

This is a retrospective study with a small sample of patients in relation to the duration of the study (8 patients), missing data especially in terms of time to consultation and risk factors that may be incriminated such as smoking, chronic urinary tract infections, history of UTUC in the family and others.

RESULT

Of the 08 files obtained, the study showed an average age of 70.85 years, with ages ranging from 65 to 77 years, with a sex ratio of 1.66 (5 men to 3 women). 5 patients (62.5%) had a history of bladder tumours, including 3 patients (37.5%) who had a history of bladder tumours before the development of UTUC and 2 patients (25%) who had a bladder tumour discovered during UTUC surveillance.

Low back pain was noted in 04 patients (50%), haematuria in 2 patients (25%), a combination of low back pain and haematuria in 1 patient (12.5%) and an incidental finding in 1 patient (12.5%) during flexible ureteroscopy for a medium-sized calculus.

Uroscan were performed in all our patients, and ureteral lesions were diagnosed in 7 patients (87.5%), of whom 4 patients (50%) had a ureteral lesion + ureteropyelocal dilatation, and 1 patient (12.5%) had no lesion visible on CT scan.

All our patients had normal renal function. In our case series, there was no predominance of one side over the other (50% right side, 50% left side).

Cystoscopy showed:

- An infracentimetric polyp at the level of the bladder dome in 3 patients (37%), including 1 patient during surveillance for UTUC and who had no history of bladder tumour; the other 2 were already being monitored for bladder tumour.
- A trigonal polyp measuring approximately 3cm in 1 patient (12.5%) who had a history of bladder tumour.
- A subcentimetric floor polyp in 1 patient (12.5%) who had no history of bladder tumour.
- Cystoscopy normal in the other 3 (37.5%).

Ureteroscopy showed:

- A papillary lesion of approximately 1cm of the middle calyx of the right kidney in 1 patient (12.5%).
- A lesion of the pelvic ureter in 4 patients (50%), measuring approximately 1.5cm, 2cm and 3cm in the first 3 patients.
- A lesion occupying the entire pelvic ureter in the 4 ème patient.
- A lesion of the iliac ureter in 3 patients (37.5%), measuring approximately 1 cm, 2 cm and 4 cm respectively.

Urine cytology was favourable:

- Strong suspicion of high-grade urothelial lesion in 2 patients (25%).
- Appearance of low-grade urothelial lesion in 3 patients (37.5%).
- Uncertain malignancy in 3 patients (37.5%).

Pathology was favourable:

- LG Pta urothelial carcinoma in 6 patients (75%).
- Probable LG tumour in 1 patient (12.5%).
- LG Pt1a urothelial carcinoma in 1 patient (12.5%).

The decision to treat all our patients conservatively by ureteroscopy was taken by the RCP staff. TAP CT-Scan did not show any secondary locations in any of our patients.

All our patients were aware of the surgical procedure, follow-up and possible tumour recurrence requiring repeat laser vaporisation or invasive surgery such as NUT if laser electrocoagulation failed, and signed their consent.

In our series, 5 patients (62.5%) had benefited from laser vaporisation using a rigid ureteroscope compared with 3 (37.5%) patients using a flexible ureteroscope, with no preference for one over the other except for the middle calici location where the rigid ureteroscope was not indicated. The average duration of the operation for 7 patients (87%) was between 1h and 1h30min, except for 1 patient who had a diffuse tumour throughout the ureter and whose Nephroureterctomy was not discussed given the patient extensive history of ischaemic heart disease and ileofemoral bypass, and whose laser vaporisation lasted up to 2h.

Surgery was performed on an outpatient basis in 6 patients (75%), compared with a 1-day hospital stay for monitoring in the other 2 (25%), whose medical history included ischaemic heart disease, ileofemoral bypass and ischaemic stroke. No postoperative complications were noted in any of our patients.

The follow-up was marked by:

- Recurrence of UTUC at 3 months in 1 patient (12.5%).
- Recurrence of UTUC at 3 months, 9 months, 1 year and 2 years in 1 patient (12.5%).
- Ureteral and bladder tumour recurrence at 1 year in 1 patient (12.5%).
- Recurrence of UTUC tumour after 9 months in 1 patient (12.5%).
- Appearance of a bladder tumour after 1 year, without recurrence of UTUC In 2 patients (25%) who had no history of bladder tumour.

No recurrence after 1-year follow-up in 2 patients (25%).

DISCUSSION

The incidence of UTUC is low: 1 to 2 cases/100,000 inhabitants per year, i.e. 5 to 6% of urothelial carcinomas, with a much lower prevalence compared with kidney and bladder tumours [3]. The incidence of UTUC is undoubtedly lower than that of kidney or bladder tumours, as over a 3-year study period we were only able to collect 8 patients with UTUC, in contrast to the larger number of bladder or kidney cancers that we encountered in our practice at the HNFC.

These tumours are exceptional in children and adolescents. They are predominantly male, with a sex ratio of between 3 and 4 [4]. The mean age of discovery in our study was 70.85 years, with a sex ratio of 1.66. In the study by Benchekroun A *et al*., the mean age was 65 years, with a sex ratio of 3 [4]. In the study by Djokic M *et al*., the mean age was 63 years, with a sex ratio of 1.3 [5].

Ureteral tumours are more rapidly invasive than pyelic or caliceal tumours. Metastases occur mainly in bone (30%), lung (25%) and liver (20%) and are observed in high-grade tumours [6]; no metastases were observed in any of our patients.

According to the study by Djokic M *et al*., haematuria was the main revealing sign found in more than 80% of cases, with a similar percentage in the study by L. ELMESNAOUI *et al*., at the Mohammed VI University Hospital in Marrakech, where haematuria was found in 83% of patients [5, 6]. In our series, haematuria was present at a lower percentage than in the other two studies in 37% of our patients.

Pain in the form of low back pain or renal colic was found in 20 to 30% of patients in the same study by Djokic M, with a higher percentage of around 72% found in the study by L. ELMESNAOUI *et al*., [5, 6]. In our study, lumbar pain was reported by 62% of our patients. Urinary tract infection may be asymptomatic, associated with general signs or pollakiuria. The latter may be the manifestation of a tumour of the ureter prolapsing into the bladder. In our series, the cytobacteriological examination of the urine (CBEU) was sterile in all our patients.

The gold standard for diagnosing UTUC is uroscan. The sensitivity, specificity and accuracy of uroscanner for the detection of UTUC are greater than 93% in most studies [7, 8].

However, in a study by Gallioli *et al*., the performance of CT for the characterisation and staging of UTUC was less good, with a sensitivity of only 52.1% [9].

In our study, the performance of CT scanning was 88% in the diagnosis of UTUC. According to two studies, the finding of a synchronous bladder lesion on cystoscopy is in the order of 8 to 13% of cases [2, 10, 11], in contrast to our study in which a synchronous bladder lesion was found in 62.5% of cases.

Abnormal urine cytology can raise the suspicion of high-grade UTUC when bladder cystoscopy is normal and in the absence of carcinoma in situ (CIS), the overall sensitivity is only 40 to 63% for the detection of UTUC [12].

In our study, urine cytology was abnormal in all our patients, even in the 3 who had normal cystoscopy.

Ureteroscopy (URS) can be used to explore virtually the entire upper urinary tract [10] and to biopsy suspicious lesions. The real added value of URS compared with CT scan is the characterisation of UTUC.

The URS therefore plays an important role in risk stratification, while the site of the lesion influences the possibility of conservative treatment [9].

According to the latest recommendations from the French Association of Urology (FAU) and the European Association of Urology (EAU) [7, 13], URS is systematically recommended when urine cytology is positive with no lesion identified on cystoscopy or imaging, when there is diagnostic doubt on imaging about a benign lesion, or when conservative treatment is being considered.

In our study, 5 patients (62%) had rigid URS, compared with 3 patients (38%) who had flexible URS.

Conservative treatment of UTUC is routinely indicated for low-risk tumours in patients with two functional kidneys, regardless of location [14]. A meta-analysis showed that conservative treatment of low-risk tumours reduced the morbidity associated with Nephroureterectomy without compromising oncological prognosis [15]. In patients with low-risk UTUC without bladder localisation, antegrade instillation of bacillus Calmette and Guérin (BCG) or mitomycin Cinto the renal cavities via nephrostomy appears to reduce the risk of local recurrence with good tolerability [16]. None of our patients had received antegrade instillations of bacille Calmette et Guérin (BCG) or mitomycin C.

The AFU recommends flexible URS laser photovaporisation as first-line treatment for low-risk UTUC. The risks of underestimating the tumour stage, as well as the risk of recurrence (6 to 71%) or progression (15 to 21% in the event of recurrence) must be known and explained to the patient [17].

Patients should be advised of the value of performing an early second look USR six to eight weeks after initial treatment [18].

The decision to treat these patients conservatively was confirmed at the RCP staff meeting, and all the patients were informed of the benefits of follow-up ureterorenoscopy and the risk of tumour recurrence, and gave their consent.

According to CCAFU 2013, the indications for conservative treatment are unifocal tumour, less than 1cm, no grade, no history of bladder tumour, no radiological evidence in favour of infiltration, close endoscopic surveillance of the patient and patient information [19].

According to the literature, bladder recurrence is described in 30 to 50% of cases, and 20 to 43% of patients with initial conservative treatment eventually underwent Nephroureterectomy, after a delay of 10-22 months [20].

ELLIOTT D. S reported a series of 44 patients treated for UTUC by electrocoagulation or laser with a mean follow-up of 5 years. Some of the tumours were grade 3 or stage T2; 40% of patients had had a local recurrence and there had been only one progression; 44% had developed bladder tumours. 14% of patients ultimately required Nephroureterectomy. 6 patients (5 of whom were also known to have an invasive bladder tumour) died of metastatic disease [21]. Cutress ML concluded from a systematic review of the literature that the rate of bladder recurrence is 30-50%, and that 20-43% of patients with initial conservative treatment eventually underwent Nephroureterectomy, after a delay of 10-22 months [20].

In our study, 3 patients (37.5%) had a recurrence of UTUC; 2 patients (25%) had developed a bladder tumour, a recurrence of bladder tumour and UTUC after 1 year was noted in 1 patient (12.5%), 1 patient (12.5%) finally required a segmental ureterectomy after 1 year, 2 patients (25%) had no recurrence after 1 year control, and no case of death was noted in our series.

CONCLUSION

UTUC are uncommon tumours, with a predominance of men over the age of 50. The risk factors and histological types are similar to those of bladder tumours. Multifocality is common, and uroscanner coupled with endourology is the key diagnostic test. Ureterorenoscopy remains the reference technique for the conservative treatment of UTUC, but requires strict monitoring because of the risk of recurrence.

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