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DIODE LASER FOR THE MANAGEMENT OF UPPER TRACT UROTHELIAL CANCER (UTUC) – CASE SERIES

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Abstract

Background and Objective: Upper tract urothelial carcinoma (UTUC) is uncommon; however, at the time of diagnosis, they are usually more invasive than bladder urothelial carcinomas. Although nephroureterectomy (NU) has been the gold-standard treatment, guidelines have been set for kidney-sparing treatment in selected groups of patients. While these guidelines are aimed towards patients fit for salvage radical treatment, little has been published on managing the symptomatic patient not fit for NU. Various modalities of endoscopic ablation in managing UTUC have been described in the literature, but there is currently no reported use of the diode laser. Therefore, we aim to assess its efficacy and safety profile in the ablation of UTUC in patients unfit for major abdominal surgery in radical nephroureterectomy regardless of the tumour grade and size.

Patients and method: A single centre retrospective review of patients who underwent Diode Laser treatment for UTUC over 4 years was done. Follow up through 6 monthly ureteroscopy alternating with computed tomography (CT) urogram was done to assess the need for further treatment.

Results: 30 patients were identified, with mean age 76 years (64-88) and variable tumour locations, including lower and mid ureter and renal pelvis, upper and lower calyces. 76.7% were ASA 3 and 20% ASA 4. The mean tumour size was 3.8 cm (2-7 cm). The mean number of sessions was 2.1 (1-6). 63.3% of the tumours were grade 2, while 30% were grade 3. A case of metastatic renal-cell carcinoma was diagnosed as a 4 cm filling defect in the kidney where the diode laser was used for resection biopsy and ablation. 16.7% experienced Clavien-Dindo grades 1-2 complications. A total of 6.7% of patients were converted to an inpatient stay. None of the patients needed blood transfusion nor did any develop a ureteric stricture on subsequent ureteroscopies. 48.3% of patients experienced clinical recurrences of which 57.1% were at a different site. Two of the patients developed metastatic disease. One patient died 3 years after initial treatment with disease progression.

Conclusion: The management of UTUC with diode laser is a safe and efficacious conservative treatment for disease and symptom control in patients unfit for radical treatment.

Keywords: *diode laser, upper tract urothelial cancer (UTUC), kidney sparing, palliative*

INTRODUCTION

Upper tract urothelial carcinoma (UTUC) is uncommon and accounts for 5 to 10% of all urothelial cancers, with a yearly incidence of 2/100 000 population in developed countries.[1] UTUC refers to malignant changes of the urothelium extending from the distal ureteric orifice to the renal calyces. At the time of diagnosis, UTUCs are usually multifocal and more advanced than bladder urothelial carcinomas making them more invasive.[2]

Although radical nephroureterectomy (NU) has been the gold-standard treatment for UTUC, endoscopic management has been used in selected cases. The European Association of Urology (EAU), in published guidelines, has recommended kidney-sparing management as the primary treatment option for low-risk tumours (unifocal, <2 cm, low grade, and no evidence of invasion on CT) and patients with solitary kidney and/or impaired renal function providing that it will not compromise survival.[3] Some comparative studies have shown similar 5-year cancer-specific survival for NU and patients managed with endoscopic ablation.[4–6]

Variations in endoscopic ablation of UTUC continue to evolve because of the continuous advances in the endoscopic armamentarium. Previously, the most frequently used lasers in managing UTUC were the holmium yttrium aluminum garnet (Ho:YAG) and the neodymium yttrium aluminum garnet (Nd:YAG); however, increasing success has been reported with the thulium laser in recent years.[7–11] Despite the differences in laser properties, no study has shown the superiority of one laser type over the other. In addition, there are currently no published data on the use of the diode laser in managing UTUC.

Whilst the guidelines are clear regarding managing patients with UTUC who will benefit from NU if kidney-sparing management fails, little is documented on managing patients who may not be fit for radical surgery. These patients can be challenging to manage, requiring frequent hospitalizations due to ongoing symptoms from bleeding, pain and/or obstruction.

AIMS

To assess the efficacy and safety profile of using diode laser for ablation of UTUC in patients unfit for major abdominal surgery in the form of radical nephroureterectomy regardless of the tumour grade and size. In addition, we considered the impact of repeated short general anaesthetic, the disease control achieved, the development of complications, disease progression, and the optimal follow-up regime in these patients.

METHODS

A single-centre retrospective review of the database for patients who had ureteroscopic Diode Laser ablation of UTUC over 4 years between June 2016 and December 2020 was performed. Data on patients' fitness, including comorbidities and American Society of Anaesthesiologists physical status scores (ASA), was collected. The tumour grade, stage, type, number, size, and location were also assessed. Postoperative analgesia, admissions, and complications were reviewed for all patients.

SURGICAL TECHNIQUE

All Cases had pre-procedure ureteroscopy and Biopsies (Except the case with metastatic Renal cell carcinoma). All cases were discussed at Urology multidisciplinary team meeting (MDT) and had an anaesthetic assessment performed by a senior anaesthetist including Cardio Pulmonary Exercise Test to assess their fitness for radical treatment. Patients were offered either diode laser ablation as a palliative option or watchful waiting. All patients were operated on by the same surgeon. The operative time was limited to 60 minutes in all cases.

All patients were listed as day cases. A sensor guidewire was inserted into the affected side. Rigid ureteroscopy was done for lower and middle ureteric tumours, while flexible ureteroscopy was done for the rest of the upper urinary tract. A 10–12F access sheath was used to reduce the intrarenal pressure when a flexible ureteroscopy was done. The diode laser was set to emit 2 W output power at 1470 nm. There was no mitomycin-C used after the procedure. Anticoagulant medications were only stopped when it was deemed safe at preoperative assessment and continued in high-risk patients. Postoperative pain was managed with a 5-day course of paracetamol 1 g QDS and codeine 60 mg QDS.

Follow-up

Initially, the procedure was repeated on a 6 monthly basis to asses for recurrence and clearance. During the COVID-19 Pandemic, a 6 month CT urogram alternating with ureteroscopy was used as a follow-up method to determine whether further treatment was needed alongside patients' symptoms.

RESULTS

A total of 30 patients with ureteric or renal transitional cell cancer and 1 with a solid renal pelvic lesion (which turned out as metastatic RCC), unsuitable for radical nephroureterectomy, underwent ureteroscopy, biopsy, and diode Laser ablation in the period June 2016 - December 2020. The mean patient age was 76 years at the time of diagnosis (range 64-88). They all had American Society of Anaesthesiologists physical status scores (ASA score) calculated (see table below). Although ASA grade 2, one patient was offered endoscopic management due to a solitary kidney.

All patients had at least three or more of the flowing recorded comorbidities: left ventricular systolic dysfunction, atrial fibrillation, Reynaud disease, obesity, herniated spinal disc, Myocardial Infarction, cardiac defibrillator, chronic obstructive pulmonary disease, congestive cardiac failure, diabetes mellitus, transient ischaemic attack, chronic kidney disease; stage 3B or more, dialysis, pernicious anaemia, hypertension, cardiac stents, gastro-oesophageal reflux, pacemaker, Lynch syndrome.

The tumours were present in the mid and lower ureter and renal pelvis, upper calyx, and lower calyx. 40% of tumours were ureteric while 60% were renal.

TABLE 1 Patients' ASA Grade 1

ASA score	Number of patients
1	0
2	1
3	23
4	6

The median follow-up period was 30 months. The mean tumour size was 3.8 cm (range 2–7cm). The tumour was low grade in 44.8% of cases. The number of treatment sessions varied from 1-6 sessions (mean 2.1). There was a reduction in tumour size in all cases. On follow-up ureteroscopy, 51.7% of patients were noted to have achieved complete tumour clearance after their initial treatment. Clearance has been maintained on subsequent follow-up urograms. However, 48.3% of patients experienced recurrences, 57.1% at a different site to the primary tumour. Two cases developed distant metastasis; one with high-grade disease and the second with low-grade disease. The data is represented in Table 2.

A single metastatic renal cell carcinoma on immunotherapy in the right kidney was initially diagnosed with a 4 cm filling defect in the left kidney. The diode laser was used for resection biopsy and lesion ablation. The laser settings, in this case, were different using 2 watts of 980 nm for the resection biopsy then 2 watts of 1470 nm to ablate the lesion. The subsequent histology showed the lesion to be a metastatic RCC. There was no need for further endoscopic management as the patient continued on immunotherapy and showed no evidence of recurrences in subsequent scans at the ablated site.

One patient with grade 3 upper calyx TCC received no benefit from the endoscopic management of the tumour due to repeated significant contact bleeding resulting in very poor vision during the procedure preventing any significant reduction in tumour size. After 3 ureteroscopy attempts, including one failed attempt of chemo-resection using mitomycin C, the decision was taken to offer no further endoscopic management and refer onward for palliative immunotherapy due to possible small lymph node metastasis (less than 1 cm). Repeat CT urogram in 3 months showed an increase in tumor size by 1cm and lymph nodes metastases despite immunotherapy.

One case had a low-grade, low-stage tumour on all biopsies but had chest nodules which were kept under observation. The patient developed a lesion anterior to the sternum confirmed on biopsy as metastatic TCC and was referred for palliative

TABLE 2 Tumour Characteristics, Location and Number of Sessions

Patient	Location	Size	Histology	Size of recurrence at first check URS 6 months	Recurrence at another site	Total number of sessions
1	distal ureter	7 cm	G2pTa	1 cm	Upper calyx	6
2	distal ureter	5 cm	G2(HG)pTa	0.5 cm	Lower calyx	2
3	distal ureter	5 cm	G2pTa	1 cm	Renal pelvis	3
4	distal ureter	4 cm	G3pTa	-	-	1
5	distal ureter	2 cm	G2pTa	-	-	1
6	distal ureter	5 cm	G3pTa	2 cm	Lower calyx	6
7	distal ureter	4 cm	G2pTa	0.5 cm	-	3
8	distal ureter	2 cm	G2(HG)pT1	-	-	1
9	mid ureter	5 cm	G2pTa	-	-	1
10	mid ureter	3 cm	G2pTa	1cm	-	2
11	mid ureter	5 cm	G3T1	1 cm	-	2
12	upper ureter	3 cm	G2(HG)pT1	-	-	1
13	renal pelvis and upper calyx	6 cm	G3pTa	4 cm	Upper calyx	6 (died from AKI and disease progression 3 years after 1st treatment
14	renal pelvis	3 cm	G2pTa	1 cm	Lower pole	3
15	renal pelvis	3 cm	G3pTa	1 cm	-	2
16	renal pelvis	3 cm	G2pTa	-	-	1
17	renal pelvis	4 cm	G2(HG)pT1	-	-	1
18	renal pelvis	2 cm	RCC	-	-	1
19	upper calyx	5 cm	G2pTa	2 cm	-	4
20	upper calyx	3 cm	G2(HG)pT1	-	-	1
21	upper calyx	2 cm	G1pTa	-	-	1
22	upper calyx	4 cm	G3pTa	1 cm	Mid ureter	4
23	lower calyx	5 cm	G2pTa	2 cm	-	2
24	lower calyx	4 cm	G2pTa	1 cm	Lower ureter	3, developed metastatic disease in chest 3 years after 1st treatment
25	lower calyx	3 cm	G2(HG)pT1	-	-	1
26	lower calyx	3 cm	G2(HG)pT1	-	-	1
27	lower calyx	3.5 cm	G3pTa	-	-	1
28	lower calyx	4 cm	G3pT1	-	-	1
29	lower calyx	2 cm	G2pTa	-	-	1
30	lower calyx	3 cm	G3pT1	-	-	1

AKI = acute kidney injury.

chemotherapy. The patient had a history of smoking and continued to smoke during treatment.

Postoperatively, 16.7% of patients experienced Clavien-Dindo 1 and 2 complications. These included haematuria (3.3%), haematuria, and acute kidney injury (AKI) in a patient with a single-functioning-kidney (3.3%), vomiting (6.7%) and acute urinary retention (3.3%). Only 6.7% of these patients were converted to inpatient stay (haematuria and AKI) for 2 days and managed conservatively at the ward level. None required blood transfusion. None of the patients required hospital admission for postoperative pain management nor were any cases found to have a ureteric stricture on repeated ureteroscopy or CT urogram.

There was one mortality in a patient with a single functioning kidney and chronic kidney disease stage 4, after 3 years of treatment with renal failure and disease progression.

DISCUSSION

Over the past years, various types of lasers have been used successfully in managing UTUC. However, the effect depends on the type of laser used, where shorter wavelengths result in greater heat conversion; and a high tissue absorption coefficient results in shallow penetration. Although the renal sparing approach has been recommended for managing low-risk tumours, there is no specific recommendation for managing UTUC in high-risk or patients who are unfit for radical treatment.

The diode laser is a compact and portable unit whose energy is absorbed by water and haemoglobin. This allows the diode laser to have both good haemostatic and vaporization effects at low energy levels, making it suitable for ablation therapy.[12]

Despite the multiple published series on the three most documented used laser modalities in managing UTUC (Ho:YAG, Nd:YAG and thulium), no conclusive evidence indicates the superiority of a particular laser type. The thulium laser provides a continuous wave, precise incisions, and excellent coagulation and vaporization functions while avoiding temperature increases which can lead to surrounding tissue damage.[13] The holmium laser, on the other hand, can lead to ureteral transluminal microperforations or microperforations due

FIGURE 1 Diode laser set up at our unit.

to discontinuous tear-like damage to tissues. As a result, in some series, the thulium laser has demonstrated better efficacy with few complications than the holmium laser system.[14–16]

Due to the high risk of recurrence and progression associated with endoscopic laser management of UTUC, guidelines have suggested careful and long-term follow-up.[17] One important criterion affecting endoscopic ablation's success is tumour size.[11,18] Our series showed a recurrence rate of 48.3%; however, 86.2% of our patients presented with tumour sizes greater than the recommended size eligible for endoscopic ablation. None of the patients experienced tumour progression on subsequent biopsies or imaging. There was definite reduction in all tumour sizes with a diode laser except in one case with high-grade disease. With a median follow-up period of 30 months, 51.7% of the patients experienced complete tumour response after 1 session without needing further procedures. 73.3% of these patients had tumour sizes above 2 cm and 66.7% with high-grade disease.

Laser treatment for UTUC is generally safe and well tolerated; however, the risk of perforation and ureteric stricture remains a limiting factor. In a systematic review, Chieng Hin et al. reported that complications were not uniformly reported but ranged from 7.1 to 46%, with the commonest serious complication being ureteric stricture.[19] In our series, 20% of patients experienced complications, all of which were Clavien-Dindo grades 1 and 2. Only 2 of the patients needed admission for further management. One was a CKD patient with a single kidney who developed haematuria and AKI. This patient was anticoagulated and was thought to be too high risk to discontinue anticoagulation medication. The AKI was likely due to clot colic and resolved spontaneously. The other patient was one with very friable tumours with easy contact bleeding. None of the patients required blood transfusion, and no ureteric strictures were diagnosed despite treating patients with significantly large tumours with multiple sessions. This may be attributed to the low power settings of the laser.

Although a risk-stratified approach to follow-up has been recommended for surveillance in patients managed endoscopically for UTUC, these are for patients who would benefit from radical treatment should ablation therapy fail.[20] In our cohort of patients who were already deemed unfit for radical treatment we aimed to develop the optimum follow-up protocol. The follow-up protocol was initially designed with a repeat ureteroscopic examination on 6 month basis which was well tolerated by patients. However, with the COVID-19 pandemic and the resulting reduced access to the operative theatre we shifted the follow-up to alternating 6 monthly CT urogram with ureteroscopy and eventually yearly CT urogram, with ureteroscopy being performed only if indicated.

Overall, our data shows very encouraging results for disease clearance and control for UTUC when using a low-energy diode laser in high-risk patients, with minimal complications. In addition, with a low postoperative admission rate (6.7%), we have potentially reduced the risk of frequent hospital visits by these patients due to symptoms associated with their UTUC.

CONCLUSION

In our limited Series, Diode Laser was both a safe and effective method for managing UTUC in patients unfit for radical treatment. The procedure was well tolerated by often frail and comorbid patients and allowed for disease control including in large-size tumours. Although the initial aim of the intervention was palliative, we note disease clearance in a significant proportion of patients, including those with high-risk diseases. No major complications were reported, although the number of cases in this study is still low. Based on these preliminary results, the diode laser can be considered an option alongside the thulium and holmium laser in kidney-sparing surgery for UTUC.

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