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Introduction

Transitional cell carcinoma of the ureter is a relatively uncommon condition contributing to less than 5% of all urothelial cancers with the majority (70%) occur in the lower ureter versus 25% in the mid ureter and 5% in the upper ureter [1,2]. This pattern of distribution is thought to be attributed to downstream implantation.

A propensity to multifocality and recurrence in the ipsilateral ureter, as well as a low recurrence rate in the contralateral ureter, make radical nephroureterectomy the logical Gold standard treatment [3-8]. However some patients are inherently unsuitable for nephroureterectomy; such as those with a functionally solitary kidney, renal insufficiency or multiple co-morbidities. Nephroureterectomy would impose upon these individuals the need for dialysis, or have a profound effect upon quality of life and life expectancy [9]. Furthermore patients and clinicians often hesitate at nephroureterectomy in those with low grade, unilateral tumours in the distal ureter.

In response to the difficulty posed by patients deemed unsuitable for nephroureterectomy, there have been a number of attempts to manage this condition with renal sparing and less invasive techniques including endoscopic control (for example laser ablation), or segmental ureterectomy with ureter-ureteric anastomosis. However local excision preserves the ureter distal to the primary tumour where recurrence is most common up to 50% [10]. Distal ureterectomy would theoretically reduce the risk of these distal recurrences.

In our institution the patient is placed in supine position and prepared to include the genitalia to enable catheterisation during surgery. A curvilinear Rutherford-Morris or Gibson incision is made on the affected side allowing access to the bladder and affected ureter. The ureter is then isolated as it crosses the common iliac at the pelvic brim and mobilised along its entire length. The urachus is divided and an inverted U shaped anterior peritoneotomy is made to mobilise the anterior and anterolateral aspects of the bladder in the retropubic space [11]. The bladder is then filled with saline. An anterolateral bladder flap based on the ipsilateral vesical pedicle is created in a ‘boot’ shape. The flap should be three to four centimetres longer than the defect. The affected ureter then has a standard JJ stent inserted retrograde, if one has not already been placed, and tied into the ureteric orifice with suture. The Ureteric orifice and ureter is then excised in continuity as a cuff. The proximal ureter is excised as high as possible over the stent, and a refluxing ureteroneocystostomy is created. It is our belief that this allows easier visualisation of the proximal ureter for future follow up of these patients. Mucosa to mucosa absorbable stitches are placed between the spatulated free proximal ureter and the bladder mucosa. A new JJ stent is then placed and the Boari flap tubularised in two layers. A drain is then placed in the pelvis and the abdominal wound closed as per normal.
We present a series of patients with bulky low grade distal ureteric carcinoma, managed with distal ureterectomy and Boari flap reconstruction.

Methods

A retrospective database was collected on all patients at a single hospital who had open distal ureterectomy and Boari flap reconstruction for distal ureteric transitional cell carcinoma by one surgeon. This was to replace the lower ureter in its entirety and allow tension free anastomosis.

Patients were identified using the National Health Service OPCS Classification version 4.5 unique code for distal ureterectomy, Boari flap reconstruction and ureteric reimplantation. The tumours were all distal near the bladder end and up to the pelvic brim keeping 2cm proximal margin free. The majority of tumours were 2-4cm, two were 6cm.

A retrospective review of the patient notes and investigations was made. Data was collected on patient demographics, presenting symptoms, risk factors, pre-operative co-morbidities, pre-operative estimated Glomerular Filtration Rate (eGFR), histology, recurrence and complications using Microsoft Excel 2007.

Results

Data was collected on 20 consecutive patients between 2004 and 2015 that had distal ureterectomy and Boari flap reconstruction for distal ureteric transitional cell carcinoma. The patient summary demographics, are listed in table 1. Specific patient demographics are in table 2. The histology of diagnostic biopsy, final specimen and progression and survival figures are in table 3 and 4. None of the patients were censored. Two patients died from the cancer and eight died overall. Three showed recurrence. One developed a new tumour in the other ureter.

The majority of patients presented with haematuria, 55% (11/20), 25% (5/20) were detected with bladder tumour surveillance and 20% were incidental findings (4/20). The mean length of ureter resected was 83mm. Ten patients had G2pTa, six had G1pTa, one patient had G2pT1 and three had G3pT2 disease. The mean length of follow up was 79 months (8-144 months).

Five biopsies were upgraded/staged. Three G1pTa biopsies subsequently proved to have G2pTa disease. One G3pT1 biopsy was upstaged to G3pT2 and one biopsy that showed inflammatory changes only proved to have G3pT2 disease (Graph).

Local recurrence

There were three cases of local recurrence. Three were ipsilateral ureteric tumours and one new contralateral tumour. All three high grade cases developed recurrence.

The first ureteric local recurrence (patient 1) was G1pTa and subsequently underwent radical nephroureterectomy. This was at 54 months.

The second ureteric local recurrence (patient 2) was G2pTa low grade, (34mm from the distal ureteric margin). This patient consequently had a nephroureterectomy and no further recurrence.

The third (patient 19) had a contralateral recurrence that was offered a nephroureterectomy but she opted for a laser ablation. The fourth (patient 20) developed an ipsilateral recurrence within the renal pelvis and died.

Graph: Kaplan-Meier survival/mortality all cause and disease specific with progression.

| Table 1: Summary values of patients. |
|-------------------------------------|
| Male/female | 13/7 |
| Age | Mean 71 (sd±11) median 72 |
| Side left/right | 14 left/ 6 right |
| Length of distal ureter | Mean 83mm (sd±30) |
| Creatinine pre op post op Mann Whitney P | Mean 101µM (sd±58) Mean 104 µM (sd±60) P = 0.8 |
| eGFR pre op post op Mann Whitney P | Mean 70ml/min/1.73m2 (sd±20) Mean 66ml/min/1.43m2 (sd±20) P = 0.7 |
| Presentation Haematuria | 11 |
| Surveillance | 5 |
| Incidental | 4 |
Table 2: Basic patient characteristics.

| Patient number | ASA | Age | Side  | Smoker | Presentation  | eGFR ml/min/1.73m² | Creatinine (µM) | CKD |
|----------------|-----|-----|-------|--------|---------------|---------------------|-----------------|-----|
| 1              | 1   | 64  | Right | Yes    | Haematuria    | 72                  | 75              | 2   |
| 2              | 2   | 85  | Left  | No     | Surveillance  | 53                  | 92              | 2   |
| 3              | 3   | 75  | Left  | No     | Haematuria    | 62                  | 83              | 2   |
| 4              | 1   | 69  | Left  | Yes    | Surveillance  | 56                  | 91              | 3   |
| 5              | 2   | 61  | Left  | Yes    | Surveillance  | 65                  | 82              | 3   |
| 6              | 2   | 55  | Right | Yes    | Incidental    | 86                  | 85              | 2   |
| 7              | 2   | 63  | Right | No     | Surveillance  | 77                  | 91              | 3   |
| 8              | 2   | 78  | Right | Yes    | Haematuria    | 60                  | 110             | 3   |
| 9              | 2   | 82  | Left  | Yes    | Incidental    | 62                  | 105             | 3   |
| 10             | 2   | 55  | Left  | Yes    | Haematuria    | 90                  | 82              | 2   |
| 11             | 3   | 78  | Left  | No     | Incidental    | 16                  | 339             | 4   |
| 12             | 2   | 68  | Left  | Yes    | Haematuria    | 86                  | 82              | 1   |
| 13             | 2   | 81  | Left  | Yes    | Haematuria    | 99                  | 75              | 1   |
| 14             | 1   | 56  | Left  | Yes    | Haematuria    | 55                  | 119             | 2   |
| 15             | 2   | 77  | Left  | Yes    | Haematuria    | 86                  | 129             | 3   |
| 16             | 3   | 88  | Left  | Yes    | Surveillance  | 48                  | 129             | 3   |
| 17             | 3   | 81  | Left  | No     | Haematuria    | 89                  | 77              | 1   |
| 18             | 1   | 69  | Left  | Yes    | Incidental    | 89                  | 70              | 1   |
| 19             | 1   | 57  | Right | No     | Haematuria    | 89                  | 67              | 1   |
| 20             | 3   | 87  | Right | No     | Haematuria    | 58                  | 80              | 3   |

Table 3: Biopsy, operative histology and outcomes.

| Patient | Biopsy | Final histology | Recurrence | All cause mortality | Disease specific mortality |
|---------|--------|-----------------|------------|---------------------|----------------------------|
| 1       | G1pTa  | G1pTa ipsilateral ureter | No         | No                  | No                         |
| 2       | G1pTa  | G2pTa ipsilateral ureter | yes        | No                  | No                         |
| 3       | G1pTa  | G1pTa            |            | No                  | No                         |
| 4       | G2pTa  | G2pTa            |            | No                  | No                         |
| 5       | G1pTa  | G1pTa            |            | No                  | No                         |
| 6       | Malignant? | G1pTa | No         | No                  | No                         |
| 7       | G2pTa  | G2pTa            |            | No                  | No                         |
| 8       | G1pTa  | G2pTa            |            | No                  | No                         |
| 9       | G1pTa  | G2pTa            |            | Yes                 | No                         |
| 10      | G1pTa  | G1pTa            |            | No                  | No                         |
| 11      | G2pT1  | G2pT1            |            | Yes                 | No                         |
| 12      | G2pTa  | G2pTa            |            | No                  | No                         |
| 13      | G2pTa  | G2pTa            |            | Yes                 | No                         |
| 14      | G2pTa  | G2pTa            |            | No                  | No                         |
| 15      | G2pTa  | G2pTa            |            | Yes                 | No                         |
| 16      | G2pTa  | G2pTa            |            | No                  | No                         |
| 17      | G3pT2  | G3pT2            |            | Yes                 | No                         |
| 18      | G3pT1  | G3pT2            |            | No                  | No                         |
| 19      | G1pTa  | G2pTa contralateral ureter | No         | No                  | No                         |
| 20      | Inflammation | G3pT2 | yes         | Yes                 | Yes                        |
There were three patients (17, 18 and 20) who had high grade muscle invasive disease. Patient 17 had numerous co-morbidities, obesity, diabetes, COPD, colon cancer and bladder cancer. His ASA was 3. Patient 20 had a biopsy that showed inflammatory changes only and suffered from CKD stage 3 and had an ASA of 3. The patients were offered both radical nephro-ureterectomy or distal ureterectomy and Boari flap but opted for the latter. Patient 18 developed a high grade bladder recurrence and subsequently underwent radical cystoprostatectomy.

Overall there was no significant change in the mean postoperative MDRD eGFR (66ml/min vs 70ml/min P =0.7) or in the serum creatinine (104 µM vs 101µM P =0.8).

Although there were a number of minor complications there was only one case of note of testicular atrophy.

Discussion

The incidence of upper urinary tract urothelial tumours is accepted to be approximately 1-2 new cases per 105 of the population per year, although data from the Surveillance, Epidemiology and End Results (SEER) database demonstrates an increase in ureteric tumours from 0.69 to 0.73 per 100,000 person-years between 1973 and 1996 [10,12].

Ureteric tumours occur more commonly in the lower than the upper ureter. Overall, about 70% of ureteric tumours occur in the distal ureter, 25% in the mid-ureter, and 5% in the proximal ureter [1]. This pattern of distribution is thought to be due to downstream implantation.

Although the standard treatment for distal ureteric transitional cell carcinoma has been nephroureterectomy this approach has significant postoperative morbidity and mortality [13,14]. The fact that ureteric tumours tend to occur in older patients, who now have a longer life expectancy, and the finding that with ageing there are increased risks for renal deterioration resulting from nephrosclerosis, atherosclerosis, diabetes mellitus etc, only strengthens the need for preservation of renal function and nephrons sparing surgery [15].

There have been a number of attempts to manage these patients with different strategies ranging from laparoscopic surgery to endoscopic control with varying degrees of success. Recent reports have demonstrated the feasibility of such techniques including endoscopic and percutaneous control. However the recurrence rate in the ipsilateral unit can be as high as 23-54% and cause specific mortality between 11-18% [16-28]. We feel that distal ureterectomy and Boari flap reconstruction is an improvement upon standard approaches for patients that require renal sparing surgery with isolated low grade disease at the distal ureter. It represents a more considered approach that respects the natural history of the disease and adheres to the principles required for controlling the disease. However, patient choice may dictate the decision to avoid radical nephroureterectomy.

Our patients were followed up rigorously with intravenous pyelogram, cystoscopy and ureterorenoscopy with urine cytology and upper tract cytology at three months and then six monthly for two years. For those patients whose co-morbidity precludes them from this intensive regime the time scale is adhered to but investigation includes computed tomography urogram and cystology.

The major difference between nephroureterectomy and local excision is ipsilateral recurrence which ranges from 4.8-40% [1,15,29-33]. Although most ipsilateral recurrences occur distal to the site of the original tumour, regardless of stage or grade, occasional proximal recurrences are found [10,15]. Our series compares favourably with these quoted figures (Figures 1, 2 & 3).

Regarding oncological outcomes after conservative treatments we note that there is evidence that distal ureterectomy is as effective and safe as radical nephroureterectomy in terms of cancer specific survival, recurrence free survival and metastasis free survival [34]. Other studies showed no difference in overall survival, cancer specific survival and intravesical recurrence free survival [35-37]. Neither is there any significant deterioration in renal function post operatively similar to a multi-institutional study comparing radical and conservative surgeries [38].
In excising the distal ureteric transitional cell carcinoma in continuity we also take a larger than normal segment of proximal ureter as well as completely excising the distal ureter and ureteric orifice. A standard Boari flap enables us to make up this substantial defect where a psoas hitch would be inadequate. This is reflected in the average length of ureter being 85 mm on histological specimen examination with a maximum of 15.5mm. We do a direct anastomosis orifice. A standard Boari flap enables us to make up this substantial continuity we also take a larger than normal segment of proximal

Conclusion

There are a group of patients who having developed an isolated distal ureteric transitional cell carcinoma are unsuitable for nephroureterectomy due to co-morbidity or the need to conserve nephrons. In such cases there are a number of techniques, all of which by the comparative rarity of the disease have minimal evidence to recommend them. We suggest distal ureterectomy and Boari flap reconstruction in our series is at least comparable to these techniques. Accepting the limitations of this series the results appear favourable in our institute.

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