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LETTER TO THE EDITORS

Long-term outcomes after deceased donor renal transplantation in patients with genitourinary tuberculosis

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Dear Sirs,

Tuberculosis (TB) remains a worldwide disease with a higher prevalence among the immunocompromised and lower socio-economic classes. It is the second most common cause of death from an infectious disease after HIV/AIDS [1]. The emergence of drug-resistant strains has ensured persistence of the disease for the foreseeable future [2]. Notably, the kidney is the most frequent target for disseminated disease and untreated genitourinary TB will inevitably lead to end-stage renal failure (ESRF) and death [3]. The incidence of TB is 20-fold greater in renal transplant recipients compared with the general population, and the treatment of TB in renal transplant recipients is well described [4]. Importantly, there are a paucity of studies that investigate the safety and long-term outcomes of renal transplantation in patients with ESRF secondary to genitourinary TB [5]. Herein, we describe our experience of renal transplantation in patients with ESRF specifically because of genitourinary TB.

Between January 1985 and March 2013, 3741 kidney transplants were performed in our unit, including 11 (0.15%) in patients (nine male and two female) with ESRF secondary to TB of the genitourinary tract. Their relevant demographics are described in Table 1, and the mean age at renal transplantation was 52 ± 7 (range: 41–63) years. The latency period between pulmonary TB and a diagnosis of ESRF secondary to genitourinary TB was 35.8 ± 5.5 (range: 23–40) years. Presenting symptoms included haematuria, chronic urgency, persistent flank pain, suprapubic pain, and recurrent urinary tract infections (UTIs) not responding to treatment. The duration of presenting symptoms prior to genitourinary TB diagnosis was 17.5 ± 8 (range: 10–34) months. All the patients undergoing deceased donor transplantation were diagnosed with genitourinary TB based on positive urine culture, radiological investigations, and biopsies of the genitourinary tract. Pre-transplant urological surgery was performed 5.6 ± 7.9 (range: 1–26) years pre-operatively and included removal of the genitourinary tract [i.e. removal of the kidneys, ureters, bladder, prostate (in males), and urethra] with ileal conduit formation for anticipated transplant ureteric reimplant in six patients, bilateral native nephrectomies in three patients and unilateral nephrectomy in the remaining two patients (Table 1). Pre-operatively, two patients also underwent ileocystoplasty and colocystoplasty, respectively.

All the patients were commenced on medical chemotherapy for TB 10 months prior to transplantation which included isoniazid, rifampicin and pyrazinamide for 2 months followed by isoniazid and rifampicin for the remaining 8 months [6]. During the perioperative period, all the patients were immunosuppressed with a regimen of cyclosporine (CYA), steroids and azathioprine. After 2002, patients were immunosuppressed with prednisone, tacrolimus and mycophenolic acid mofetil. All the patients also received standard antiviral, antifungal and *Pneumocystis* prophylaxis. Postoperatively, all the patients were treated with isoniazid (300 mg) and pyridoxine (20 mg) daily for 1 year and maintenance immunosuppression. Outpatient visits consisted of regular chest X-rays and early morning urine samples for Ziehl–Neelson staining and polymerase chain reaction (PCR) analysis (after 2003) to rule out TB recurrence at 6 monthly intervals. Finally, liver function tests (LFTs) were performed monthly for the first 3 months and 3 monthly thereafter until the postoperative course of TB prophylaxis was completed.

The mean duration of long-term follow-up was 175 (12–252) months. Among the 11 patients transplanted, four are alive with a functioning kidney after a mean of 185 (90–252) months and their serum creatinine is 113 ± 23 μmol/l. Five patients died with a functioning graft after a mean of 160 (12–254) months. Causes of patient mortality are outlined in Table 1, and the serum creatinine in this subgroup was 152 ± 79μmol/l. Only one patient (Table 1: Patient number 5) suffered reactivation of TB after 2 months despite undergoing pre-operative removal of the genitourinary tract with ileal conduit formation prior to renal transplantation. Acid-fast bacilli were detected on bone marrow biopsy and this patient was commenced on full dose anti-TB chemotherapy (isoniazid, rifampicin, ethambutol and pyrazinamide). Renal allograft function was maintained during the reactivation process and his maintenance immunosuppression regime remained unaltered. Two patients

Table 1. Demographics of patients undergoing renal transplantation with end-stage renal failure (ESRF) secondary to genitourinary TB.

Patient No.	Age at tx	Gender	Presenting urological symptoms	Latency period between pulmonary TB and ESRF secondary to genitourinary TB (Years)	Urological surgery pretransplant	Type of dialysis pretransplant	Duration of dialysis pretransplant (months)	Last serum creatinine (μmol/L)	Duration of follow-up (months)	Long-term outcome
1	52	M	Haematuria	34	Genitourinary tractectomy and ileal conduit	Heamodialysis	5	111	192	Alive: functioning graft
2	43	M	Chronic urgency	37	Bilateral nephrectomy	Peritoneal	15	146	204	Alive: functioning graft
3	58	F	Recurrent UTIs not responding to treatment	40	Left nephrectomy	Haemodialysis	58	95	252	Alive: functioning graft
4	53	M	Persistent flank pain	23	Left nephrectomy	Pre-emptive	0	98	90	Alive: functioning graft
5	54	M	Suprapubic pain and haematuria	38	Genitourinary tractectomy and ileal conduit	Haemodialysis	32	55	216	Reactivation of TB 2 months postoperatively RIP: Sepsis
6	41	M	Suprapubic and flank pain	40	Genitourinary tractectomy and ileal conduit	Haemodialysis	12	261	252	RIP: CVA
7	60	M	Chronic urgency	36	Bilateral nephrectomy and colocystoplasty	Haemodialysis	104	197	144	RIP: MI
8	48	F	Recurrent UTIs not responding to treatment	33	Bilateral nephrectomy and ileocystoplasty	Haemodialysis	22	121	180	RIP: MI
9	50	M	Chronic urgency and haematuria	43	Genitourinary tractectomy and ileal conduit	Haemodialysis	14	132	12	RIP: SAH
10	46	M	Chronic urgency and haematuria	34	Genitourinary tractectomy and ileal conduit	Haemodialysis	32	Dialysis dependent	150	Alive: Non-functioning graft
11	63	M	Recurrent UTIs not responding to treatment	36	Genitourinary tractectomy and ileal conduit	Haemodialysis	27	Dialysis dependent	228	Alive: Nonfunctioning graft

CVA, cerebrovascular accident; MI, myocardial infarction; SAH, subarachnoid haemorrhage.

are alive after 189 (150–228) months but required a transplant nephrectomy despite a steroid boost because of rejection after 3 weeks and 22 months, respectively (Table 1; patients 10 and 11). Two further patients (Table 1; patients 1 and 2) also required a temporary steroid boost to preserve the renal allograft postoperatively. No patients experienced hepatic impairment secondary to TB and immunosuppressive chemotherapy.

Despite attempts at eradication, the incidence of TB remains high with a recent global resurgence because of multidrug-resistant (MDR) strains [7]. Worryingly, the incidence of TB among transplant recipients is as high as 6.5% in some centres in the United States [4]. Genitourinary TB accounts for approximately 1% of all the cases of TB and its prevalence also remains elevated [8]. Symptoms of genitourinary TB can appear up to 40 years after the primary infection and treatment options remain severely limited in this patient group if chemotherapy fails and ESRF ensues [9]. In the present study, our main finding is that renal transplantation represents a viable therapeutic treatment option for the patients with ESRF secondary to genitourinary TB.

A number of secondary findings were also noted. In our case series, only one patient suffered reactivation of TB after a mean follow-up >10 years despite undergoing extensive pretransplant genitourinary tract surgery. It is believed that removal of the genitourinary tract may be necessary prior to considering renal transplantation to reduce the risk of reactivation secondary to immunosuppression [10]. However, our report suggests the contrary, as removal of the kidneys, ureters, bladder prostate and urethra did not prevent recurrence in this patient. Furthermore, five patients in our series underwent limited removal of their genitourinary tract and remain free from TB recurrence >10 years after transplantation.

As the prevalence of multidrug-resistant TB continues to increase, a concomitant increase in genitourinary TB is likely to occur. In this study, we followed 11 patients who underwent pre-operative genitourinary tract surgery for TB followed by deceased donor renal transplantation. Our results demonstrate that patients with ESRF secondary to genitourinary TB can be safely transplanted with encouraging long-term outcomes.

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Conflict of interest

The authors have no conflict of interests to declare.

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