Urological complications in renal transplantation

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ABSTRACT

Introduction: Renal transplantation has gained much wider acceptance as a treatment option for local patients with end-stage renal failure in the last three decades. However, there are no local reports regarding the associated urological complications and their management. This paper aims to explore these complications in the local setting.

Methods: This is a retrospective review of 440 consecutive renal transplantations performed in Singapore General Hospital over a ten-year period. From the retrieved clinical records of transplant recipients, the occurrence of various urological complications and their management were studied.

Results: The overall incidence of urological complications among transplant recipients was 7.7 percent. Urological complications included urinary leakage, ureteric strictures, symptomatic lymphocoeles, malignancies, urolithiasis, double-J stent fragmentation as well as haemorrhagic cystitis, and their incidences were 1.4 percent, 2.0 percent, 1.8 percent, 2.3 percent, 0.2 percent, 0.2 percent and 0.2 percent, respectively. Among the malignancies, 70 percent were renal cell carcinomas in the native kidneys.

Conclusion: The incidence of urological complications in our series was comparable to those in the various major centres. However, there was a significantly higher incidence of native renal cell carcinoma in our series, which was likely to be secondary to the prolonged period of dialysis prior to renal transplantation.

Keywords: kidney transplantation, postoperative complications, renal cell carcinoma, urological complications

Singapore Med J 2006; 47(5):388-391

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INTRODUCTION

Many reports regarding urological complications in renal transplantation have been published by various major centres worldwide. However, no local report is available. Since renal transplantation has gained much wider acceptance as a treatment option for local patients with end-stage renal failure in the last three decades, it is important to have some local data regarding the associated urological complications and their management. We reviewed all renal transplantations performed in our centre over a ten-year period to explore the various urological complications in the local setting.

METHODS

This is a retrospective review of 440 consecutive renal transplantations performed in Singapore General Hospital between January 1993 and December 2002. The clinical records of the transplant recipients were retrieved and analysed. Preoperatively, all donors and recipients underwent tissue typing (human leukocyte antigen [HLA] complement-dependent cytotoxicity crossmatch and anti-kappa human globulin crossmatch). All first transplant grafts were placed in the right iliac fossa, while most repeat transplant grafts were placed in the left iliac fossa. The majority of the recipients were immunosuppressed with a combination of cyclosporin, azathioprine and corticosteroids.

Revascularisation of the graft was carried out in a standardised manner. The graft renal vein was anastomosed to the native external iliac vein in an end-to-side fashion. The graft renal artery was anastomosed to the native external iliac artery in an end-to-side fashion in most cases. Alternatively, the native internal iliac artery was used, with an end-to-end anastomosis. A modified Lich-Gregoire technique of extravesical ureteroneocystostomy was used for establishing urinary continuity. The bladder was filled with isotonic normal saline solution via a Foley catheter. An incision was placed over the anterior part of the dome and a small opening was made in the mucosa. The graft ureter was trimmed,

Table I. Demographical details of the 440 transplant cases.

	No. of transplants	No. of males	No. of females	Male:female ratio	Age range (in years)	Mean (in years)	1st:2nd:3rd transplant
Cadaveric	348 (79.1%)	174	174	1:1	15.6-59.2	42.1	333:13:2
Living-donor	92 (20.9%)	53	39	1.36:1	8.0-51.1	33.5	90:2:0

assessed for a good vascularity, and spatulated at the end before anastomosis. Routine double-J ureteric stenting was performed in all cases. Post-operatively, Foley catheters and pelvic drains were usually removed by the fifth postoperative day (POD 5), and most recipients were discharged on POD 7. Skin staples were removed on POD 10 and double-J stents on POD 14 under local anaesthesia on an outpatient basis.

RESULTS

In a total of 440 cases, there were 348 cadaveric transplants (79.1%) and 92 living-donor transplants (20.9%). Among the cadaveric group, there were 174 male recipients and 174 female recipients (gender ratio, 1:1), with a mean age of 42.1 years (range, 15.6 – 59.2 years). Among the living-donor group, there were 53 male recipients and 39 female recipients (gender ratio, 1.36:1), with a mean age of 33.5 years (range, 8 – 51.1 years). There were 333 first, 13 second and two third transplants in the cadaveric group, and 90 first and two second transplants in the living-donor group. The demographical details of the cases are summarised in Table I.

There were 36 urological complications in 34 transplants, constituting an incidence of 7.7% and affecting 34 patients, of which 18 were males and 16 were females. Of the 34 complicated transplants, 30 were cadaveric and four were living-donor transplants. There were six cases of urinary leakage as well as nine cases of ureteric stricture. There were eight cases of lymphocoele producing extramural compression. A total of ten cases of malignancies were recorded. One patient developed urolithiasis in the graft kidney, one patient had a fragmented double-J ureteric stent, and one patient had haemorrhagic cystitis.

There were six cases of urinary leakage (incidence, 1.4%), constituting 16.7% of all urological complications. All of them occurred within one month of transplantation. Five of them involved the ureteroneocystostomy site. One patient was treated successfully with cystoscopy and re-insertion of the double-J ureteric stent. One patient developed wound dehiscence and underwent an exploratory laparotomy, and open re-insertion of the double-J stent was performed after the intraoperative finding of an urinoma. One patient developed an acute abdomen after several days of generalised abdominal discomfort and low grade temperature, so she underwent an exploratory laparotomy in which turbid fluid accumulation around the graft kidney and breakdown of the ureteroneocystostomy was found. She died of fulminant sepsis about 72 hours later. One patient was treated successfully with computed tomography (CT)-guided aspiration of the urinoma. One patient developed a psoas abscess, which was successfully drained with ultrasound-guided Cope loop insertion. One patient developed a calyceal-cutaneous fistula secondary to an inadvertent perforation from guide-wire placement intraoperatively, and he underwent an ultrasonography-guided percutaneous nephrostomy.

There were nine cases of ureteric strictures (incidence, 2%), constituting 25% of all urological complications. All of them were confined to the distal portion of the ureters. Three of them were successfully treated endourologically in the form of percutaneous nephrostomy, antegrade balloon dilatation and double-J ureteric stenting. Initial attempts were made to treat two cases endourologically but failed, and these were converted to open reconstruction with Boari flap. Three of them were managed directly by Boari flap reconstruction, and the last case was managed with a simple ureteric re-implantation.

There were eight cases of extramural compressions from lymphocoeles (incidence, 1.8%), constituting 22.2% of all urological complications. They presented with hydronephrosis and oedema of the lower limbs and scrotum. In all the cases, lymphocoeles formed near the lower pole of the graft kidneys, overlying the iliac vessels. One case was treated by open drainage, two by open fenestration into peritoneal cavity, one by laparoscopic fenestration, three by CT-guided needle aspiration, and one by CT-guided Cope loop insertion.

There were ten cases of malignancies (incidence, 2.3%), including seven cases of renal cell carcinoma (RCC) of the native kidney (incidence of 1.6%), one case of RCC of the graft kidney, one case of transitional cell carcinoma (TCC) of the bladder, and one case of post-transplant lymphoproliferative disorder (PTLD) involving the adrenal gland. These constituted 27.7% of all urological complications. All

Table II. Incidence of various urological complications.

Complications	Number of cases	Incidence (%)	Percentage of all urological complications (%)*	Remarks
Urinary leakage	6	1.4	16.7	1 death from peritonitis and fulminant sepsis
Ureteric strictures	9	2.0	25.0	
Symptomatic lymphocoeles	8	1.8	22.2	
Malignancies	10	2.3	27.7	7 cases were native renal cell carcinoma (percentage 70%, incidence 1.6%)
Urolithiasis	1	0.2	2.8	
Fragmented double-J stent	1	0.2	2.8	
Haemorrhagic cystitis	1	0.2	2.8	

* A total of 36 urological complications in 34 transplants (30 cadaveric; 4 living-donor) involving 34 patients (18 males; 16 females)

seven cases of RCC of the native kidney underwent radical nephrectomy. They remained tumour free for a mean follow-up period of 47.8 months (range, 8 – 107 months). The case of RCC of the graft kidney was incidentally diagnosed by histopathological examination after graft nephrectomy for chronic rejection 15 months after transplantation. The case of bladder TCC was diagnosed nine years after transplantation. Histology showed a high-grade, muscle-invasive TCC. Radical cystectomy was performed but the patient died from extensive recurrent local disease eight months after diagnosis. The case of PTLD of the adrenal gland was treated with Rituximab immediately upon histological diagnosis.

There was one case of urolithiasis in the graft kidney (incidence, 0.2%). This patient presented with microscopic haematuria and recurrent urinary tract infection. On investigation, a 2-cm stone was found in the renal pelvis. She underwent one session of extracorporeal shockwave lithotripsy (ESWL) which showed poor result, and subsequently underwent a ureteroscopy with laser lithotripsy to clear the remaining stone fragments. There was one case of fragmentation of the double-J ureteric stent (incidence, 0.2%). The patient, who remained asymptomatic, defaulted the appointment for removal of the stent till two months after transplantation. Upon removal of the double-J ureteric stent, it was noted to be fragmented. The proximal fragment was then successfully retrieved with flexible ureteroscopy. There was one case of haemorrhagic cystitis (incidence, 0.2%). The patient presented with severe gross haematuria and clot retention, requiring two pints of packed cell transfusion and manual bladder washout. The various urological complications are summarised in Table II.

DISCUSSION

The overall incidence of urological complications in our series was 7.7%, which was comparable to those reported by other major centres (range, 5.6% – 8.3%)[1-4]. The incidence of urinary leakage was 1.4%. The incidences of urinary leakage in other major centres ranged from 0% to 8.9%[1]. There are many causes of urinary leakage, but vascular insufficiency is probably the fundamental cause of ureteric necrosis or slough with subsequent urinary extravasation[5]. Our transplant surgeons were meticulous in avoiding dissection of the renal hilum during harvesting to better preserve the vascular supply of the distal ureter, and efforts were made to obtain sufficient ureteric length to avoid unnecessary tension at the site of ureterovesical anastomoses. Politano-Leadbetter ureteroneocystostomy[6], which is a common technique for restoring urinary continuity in many overseas centres, was not used in our centre because of the multiple cystostomies created and the possibility of distal ureteric ischaemia and necrosis from a tight submucosal tunnel. Moreover, there was routine use of double-J ureteric stents, which have been shown to significantly reduce ureteric complications[7].

The incidence of ureteric stricture was 2%. The incidences of ureteric stricture in other major centres ranged from 0% to 12.4%[1]. As all the strictures in our series occurred in the distal ureter, it seemed that ischaemia was the most likely cause. However, there are papers that suggest an immunological cause. Faenza et al observed that a significant number of patients with ureteric strictures had either acute or chronic graft rejections, and they hypothesised that ischaemia should lead to early postoperative urinary leakage instead of ureteric strictures[8]. In our series, there were no graft rejections among those with strictures. Kashi et al had similar findings as our series and they also observed that the age of the donors and recipients, degree of HLA loci mismatch and use of cyclosporin had no impact on the incidence of ureteric complications[9]. Although we cannot exclude graft rejection as a cause of ureteric strictures, we believe that ischaemia is still a leading cause.

The incidence of symptomatic lymphocoele was 1.8%. The incidences of symptomatic lymphocoele in other major centres ranged from 0.6% to 18%[10]. The cause of lymphocoeles is usually leakage from the host lymphatics instead of from the graft

kidney, as shown by lymphangiography[11] as well as by labelled colloid[12]. The close proximity of the lymphocoeles to the iliac vasculature in our series also supported the idea of a host source. Nonetheless, we minimised dissection near the renal hilum during harvesting and dissection of the recipients' peri-iliac lymphatics during transplantation. Suture ligation was preferred and overuse of diathermy in the peri-iliac region was avoided, as this has been shown to reduce lymphocoele formation postoperatively[13].

The incidence of malignancies was 2.3%. The incidences of malignancies in other major centres ranged from 2.5% to 12.2%[14]. The type of malignancies in our series were rather different from those in some Caucasian series. 70% of our cases were native renal RCC. Danpanich and Kasiske showed that lymphoma constituted 18.2% of the malignancies in their series of 1,500 patients, followed by lung cancer which constituted 17%, while renal tumours only made up 3.4%[14]. The most important reason for our high occurrence of native RCC is believed to be the long duration of dialysis prior to renal transplantation. Dunnil et al first observed a relationship between haemodialysis, acquired cystic kidney disease (ACKD) and RCC[15], and Chandhoke et al found that the longer the duration of haemodialysis, the higher the incidence of ACKD[16]. It is controversial whether renal transplantation may result in regression of ACKD[17,18]. However, the incidence of native RCC in our series (1.6%) is significantly higher than that in the general population, which, based on the Singapore Cancer Registry 1998-2002, is approximately 3.9 cases per 100,000 (0.0039%).

Other urological complications included urolithiasis in the graft kidney, double-J ureteric stent fragmentation and haemorrhagic cystitis. Rhee et al reported an incidence of upper tract urinary stone of 0.23%[19], similar to that of ours. The isolated case of stent fragmentation was attributed to patient factor. No causes had been found for the case of haemorrhagic cystitis.

In conclusion, the overall incidence of urological complications in our series was comparable to those in the various major centres. The incidence of urological malignancies in transplant recipients in our series was slightly lower than those in other centres, but we have a significantly higher proportion of native RCC. This is believed to be secondary to the long duration of dialysis prior to transplantation. Immunosuppression may play a less significant role since we use similar immunosuppressants as the other centres. With increasing public acceptance of living-donor renal transplantation and better donor nephrectomy techniques, there is an increase in living-donor transplants in recent years. The recently revised Human Organ Transplant Act has also increased the number of grafts available for transplant. Hopefully, these measures will shorten the duration of dialysis prior to transplantation and subsequently decrease the incidence of native RCC among transplant recipients. Meanwhile, meticulous surgical techniques in harvesting and transplantation, especially in ureterovesical anastomosis, should be practised to minimise the incidence of other urological complications.

ACKNOWLEDGEMENT

We would like to express our gratitude to the Department of Renal Medicine, Singapore General Hospital, for the assistance provided in data collection.

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