Brief Report

Kidney transplantation after liver transplantation

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ABSTRACT: Kidney transplantation after liver transplantation (KALT) offers longer survival and a better quality of life to liver transplantation recipients who develop chronic renal failure. This article aimed to discuss the efficacy and safety of KALT compared with other treatments. The medical records of 5 patients who had undergone KALT were retrospectively studied, together with a literature review of studies. Three of them developed chronic renal failure after liver transplantation because of calcineurin inhibitor (CNI)-induced nephrotoxicity, while the others had lupus nephritis or non-CNI drug-induced nephrotoxicity. No mortality was observed in the 5 patients. Three KALT cases showed good prognoses, maintaining a normal serum creatinine level during entire follow-up period. Chronic rejection occurred in the other two patients, and a kidney graft was removed from one of them. Our data suggested that KALT is a good alternative to dialysis for liver transplantation recipients. The cases also indicate that KALT can be performed with good long-term survival.

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KEY WORDS: **liver transplantation; kidney transplantation; chronic renal failure; calcineurin inhibitor**

Introduction

In recent years, chronic renal failure (CRF) has been acknowledged as one of the most important diseases seriously affecting the prognosis of patients with liver transplantation (LT).[1] According to reports and literature, 5%-50% of orthotopic liver transplantation (OLT) patients suffer from CRF.[2] Renal function in 90% of these patients can be restored,[2] but 2%-10% will develop end-stage renal disease (ESRD).[3] In addition, hemodialysis due to renal failure after LT also greatly increases the risk of progression to ESRD.[4] Therefore, kidney transplantation after liver transplantation (KALT) for patients with renal failure after LT is a good choice in terms of maintaining renal function and extending survival of the patient and graft. Currently, because of the high survival rates of both patients and grafts after the combined liver-kidney transplantation (CLKT), more CLKTs are performed on patients whose renal function may not recover after LT. This has led to few studies on KALT recently. Nevertheless, there is emerging data suggesting that some CLKT patients may regain native renal function, demonstrating poor utilization of renal grafts. Therefore, it is necessary to perform KALT on patients with irreversible renal failure after LT. This study aimed to assess the efficacy and safety of KALT based on the results of long-term follow-up of 5 patients as well as literature reviews.

Methods

The records of 5 patients who had undergone KALT from 2002 to 2007 (the follow-up time were at least 8 years) were retrospectively studied, together with a literature review. Informed consent was obtained from these patients and the study was approved by the Ethics Committee of Beijing Chaoyang Hospital. There were 2 men and 3 women in this series, with a mean age of 45.4 years (range 37-55) when they received kidney transplantation. The mean follow-up time is 140.6 months (range 104-160) by the end of September of 2015. An overview of these patients is shown in the Table.

Results

All patients received LT because of hepatitis B-related liver cirrhosis, drug-induced liver failure, hepatitis C-related liver cirrhosis or liver cancer. One patient got

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Table. Characteristics of recipients and donors and results

Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5
Recipient characteristics					
Age (at time of KALT) (yr)	46	51	38	37	55
Gender	Female	Male	Female	Female	Male
Time on dialysis (mon)	13	3	16	31	30
Time from liver to kidney transplantation (mon)	65	112	28	83	57
Etiology of renal failure toxicity	CNI toxicity	CNI toxicity	Lupus nephritis	CNI toxicity	Drug toxicity
Donor characteristics					
Age (yr)	23	48	55	49	41
Gender	Male	Male	Female	Male	Male
Renal transplantation type	LD	DD	DD	DD	DD
Serum creatinine (μmol/L)	57	81	72	61	88
Results					
Cold ischemia time (min)	90	470	740	370	260
Operating time (min)	210	250	235	290	230
Serum creatinine (at discharge) (μmol/L)	146	108	91	67	85
Serum creatinine (September, 2015) (μmol/L)	80	76	169	904	60
Graft survival time (mon)	126-present	156-present	160-present	130	104-present
Patient survival time (mon)	Alive	Alive	Alive	Alive	Alive
Cause of graft loss	None	None	Rejection	Obstruction & pyelonephritis	None

LD: living donor; DD: deceased donor.

hypertension and diabetes, one lymphatic tuberculosis and systemic lupus erythematosus, and another diabetes in past history. Cyclosporine (CsA), tacrolimus (FK506), mycophenolate mofetil (MMF) or combination of CsA and MMF was used as immunosuppressant. Calcineurin inhibitors (CNIs)-induced nephrotoxicity (n=3) was the main reason to receive KALT for patients, followed by lupus nephritis (n=1) and non-CNI drug-induced nephrotoxicity (n=1). There was no past history in all donors. The mean cold ischemia time was 386 minutes (range 90-740), and mean operating time was 243 minutes (range 210-290). The immunosuppressive regimen after operation was CsA+MMF+steroids (n=2) or FK506+MMF+steroids (n=3), and there was no acute rejection and surgical or infectious complication happened. One of them experienced a graft function delay lasting 15 days and recovered by hemodialysis. The level of creatinine of all patients was lower than 150 μmol/L (range 67-146) when patients were discharged. In September of 2015, the serum creatinine level in 3 patients was normal under the control of CNIs-based double- or triple-drug regimen.

One of these five patients had 23 years of lymphatic tuberculosis and 14 years of systemic lupus erythematosus. One month after KALT, the leukocyte count of the patient continued to decrease, which could not be reversed by reduction of the MMF dose. The symptom was under control after withdrawal of MMF. In 2008, the patient had micro-protein in urine; in 2013, MMF was added for proteinuria (++). Biopsy prompted chronic active antibody-mediated rejection in February of 2014 and creatinine was at 169 μmol/L in September of 2015. The patient is now taking FK506+MMF+steroids.

Another patient suffered from hydronephrosis in kidney graft and the serum creatinine increased to 436 μmol/L after discharged. Ureteral stent implantation was performed but renal dysfunction could not be reversed. Therefore, the patient received hemodialysis again. Six years later, the patient decreased the dose of FK506 herself (without the doctor's order) and then experienced hematuria and flank pain, which was relieved by adding FK506. The serum creatinine level was 766 μmol/L at that time. Three months later, the transplanted kidney was removed from this patient and her creatinine was 904 μmol/L in September of 2015.

Discussion

There is currently no definitive diagnostic criteria of the CRF after LT. Some scholars proposed a serum creatinine level ≥221 μmol/L continually after LT as diagnostic criteria of the CRF. However, serum creatinine is affected by many factors, including nutritional status, muscle mass, hepatic synthesis capacity as well as medication (such as methoxybenzyl aminopyrimidine) and therefore, serum creatinine is not able to accurately reflect the level of renal function. These factors have little influence on the glomerular filtration rate (GFR), so Sharma and others