Case Report

Combined Liver-Kidney Transplantation in a Patient with Acute Liver Failure Coexisting with Acute Renal Failure

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Acute renal failure (ARF) is common among patients with liver failure awaiting liver transplantation due to the increased waiting time for available liver grafts and extended survival from improved intensive care. The role of combined liver and kidney transplantation (LKT) in this situation is quite controversial. A case of acute liver failure (ALF) complicated with ARF is reported. Non-A, non-B hepatitis was the cause of ALF. He had hemodialysis for one month before transplantation. Combined LKT was performed because of prolonged pre-transplant hemodialysis and the potential of irreversible renal failure. Severe impairment of both native kidneys was confirmed by renal scan at 6 months after transplantation. Combined LKT may be needed for patients with acute liver failure complicated with prolonged acute renal failure.

Keywords: *Acute renal failure, Acute liver failure, Cirrhosis, Liver transplantation, Kidney transplantation*

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Liver transplantation is the last resort of treatment for patients who suffer from acute liver failure and end-stage liver diseases. Hepatorenal syndrome (HRS) and non-HRS related acute renal failure (ARF) frequently accompanies advanced liver failure due to the interplay between liver and kidney function through the hemodynamic interrelationships or the existence of primary organ diseases[1-3]. Two calcineurin inhibitors (CNI), cyclosporin and tacrolimus (FK506), have been found to be the most effective immunosuppressive drugs frequently used after liver transplantation; the reduction of acute cellular rejection and the enhancement of steroid responsive after rejection therapy has been reported[4]. However, the most significant side effect of CNI is nephrotoxicity, occurring in 40-70% of post-liver transplant patients[4]. There are many important aspects for consideration while managing liver transplantation with ARF such as the chance of renal function recovery, appropriate immunosuppressive regimen and availability of donor organs. Herein, the approach of ARF in a patient with acute liver failure complicated with prolonged renal failure is presented.

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Case Report

A 60-year-old man who has been a case of well-controlled diabetes mellitus was referred to Ramathibodi Hospital with the diagnosis of sub-fulminant liver failure. His medical illness started 2 months Before, with severe fatigue, decreased appetite, ascites, and progressive jaundice; he was admitted to a local hospital. Blood tests showed aspartate aminotransferase (AST) of 1380 IU/L, alanine aminotransferase (ALT) of 1987 IU/L, total bilirubin (TB) of 13 mg/dL, direct bilirubin (DB) of 9.4 mg/dL, alkaline phosphatase (ALP) of 196 IU/L, blood urea nitrogen (BUN) of 20 mg/dL, creatinine (Cr) of 1.1 mg/dL, negative for HBsAg,

anti-HBcIgM antibody (ab), anti-HAVIgM ab, anti-HCV ab, anti-nuclear ab, anti-smooth muscle ab, and normal ceruloplasmin and ferritin levels. One month later, he developed spontaneous bacterial peritonitis, hepatic encephalopathy, oliguria, and rising of Cr level to 6.2 mg/dL. He underwent hemodialysis 3 times per week. One month later, he was referred to Ramathibodi Hospital for liver transplantation. On admission, physical examination showed grade II hepatic encephalopathy, marked jaundice and moderate ascites. Investigation revealed AST of 82 IU/L, ALT of 49 IU/L, TB of 36.3 mg/dL, DB of 35.4 mg/dL, prothrombin time (PT) of 17.8 sec, BUN of 80 mg/dl, Cr of 6.9 mg/dl, negative of HBV and HCV PCR testing, urine specific gravity of 1.010, negative of protein and blood, and a few white blood cells and none of red blood cell in urine. Acute tubular necrosis (ATN) seemed to be the major cause of ARF. Hemodialysis was continued combining with supportive treatment. Six days after admission, he underwent combined liver and kidney transplantation (LKT) from an ABO blood group-matched and negative HLA cross-matched cadaveric donor. He received methylprednisolone 1 g intravenous (IV) infusion after reperfusion. From the 1st day post-LKT, immunosuppressive drugs including methylprednisolone, FK506 (with aimed trough level of 12-15 mg/dL) and mycophenolate mofetil (MMF) 3 cap b.i.d. were given. The final diagnosis of liver pathology was submassive liver necrosis. One week and 1 month post-LKT, BUN/Cr were 34/0.8 mg/dL and 41/0.6 mg/dL, respectively. Post-LKT period was complicated with duodenal ulcer bleeding associated with MMF and cytomegaloviral infection. MMF was discontinued and ganciclovir was treated for 4 weeks. At the 4th month post-LKT, his Cr level rose to 3.4 mg/dL. Ultrasound revealed parenchymatous changing of the native kidneys, normal appearance of the kidney graft without ureteric obstruction. Kidney biopsy was done, and the pathological diagnosis was consistent with FK506 toxicity. The dose of FK506 was reduced and enteric-coated mycophenolate sodium (EC-MPS) was added. Six months after combined LKT, he felt well with serum Cr level of 1.2 mg/dL. Renal scan with ^{99m}Tc MAG3 showed severe impaired perfusion and excretory function of both native kidneys, and prolonged cortical retention without urine seen at both renal pelvis. Additional renal scan of the transplant kidney showed good uptake, perfusion, and excretory function.

Discussion

A patient with liver failure presented here developed ARF while awaiting orthotopic liver transplantation (OLT). Pre-OLT ARF, a common complication in acute liver failure and end-stage liver disease, is frequently the ischemic-type of ATN resulted from sustained pre-renal injury, HRS, sepsis and preexisting renal diseases[1,3,5]. Intra-operative and post-operative risk factors that can worsen renal function are hemodynamic instability, volume depletion and the use of nephrotoxic drugs[1,3,5]. Pre-OLT ARF predisposes OLT recipients to increased mortality, infection and post-OLT ARF, which occurs in 17% to 95% of patients having OLT[3,5-8]. The reported case had a prolonged course of ARF and had hemodialysis for 4 weeks before undergoing liver transplantation. Simultaneous LKT was performed because of the lower chance of spontaneous renal recovery from prolonged ARF, the mandatory use of CNI after liver transplantation, and the possible chance of having pre-existing renal insufficiency in a long-term diabetic patient. With increasing disparity between the demand and the supply of donor organs, combined LKT should be used cautiously[2,3,8,9]. In general, combined LKT should be offered to patients with combined primary renal and liver failure[8]. There have never been well-defined criteria for doing combined LKT in patients with pre-OLT renal failure who did not have a prior history of chronic renal diseases. Theoretically, renal status must be confirmed to be an irreversible condition prior to the decision of combined LKT. Patients with renal dysfunction secondary to HRS, a functional renal failure, should receive a liver-only transplantation; however when patients with HRS or ATN require dialysis for more than 4 to 6 weeks, renal cortical fibrosis may develop and renal function may not recover. Under these circumstances, simultaneous LKT is recommended[2,3,8,9]. Renal biopsy should be performed to identify the definite diagnosis of renal disease and to assess for the extent of glomerular and interstitial involvement[1-3,8], however renal biopsy in patients with liver failure and severe coagulopathy is riskier than in those with normal liver function[2]. Transjugular renal biopsy is suggested to be another choice but this technique requires high expertise and is not feasible in every center[1-3,8]. Renal doppler ultrasound, renal scan and gadolinium-enhanced magnetic resonance imaging (MRI) study are suggested to substitute renal biopsy for studying cortical blood flow[8]. Although combined LKT was done in the presented patient based on clinical presentation without further investigations, irreversible loss of the native kidney function was confirmed by renal scan 6 months after combined LKT.

This finding suggests that combined LKT may be required for patients with acute liver failure coexist with prolonged acute renal failure. In the presented case, prednisolone, low-dose tacrolimus and MMF was planed for long-term immunosuppression. EC-MPS which is an enteric-coated formulation delivering mycophenolic acid was selected to avoid MMF-related gastrointestinal toxicity[10,11].

In conclusion, the incidence of pre-OLT and post-OLT ARF is rising because of several factors such as improved patient survival from advanced medical care, increasing pre-OLT waiting time, and the post-OLT use of CNI[8]. Well-defined criteria for patients who really require combined LKT is warranted due to the wide shortage of organ donation. Combined LKT may be needed for prolonged acute renal failure in patients with acute liver failure.

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การผ่าตัดเปลี่ยนตับร่วมกับการปลูกถ่ายไตในผู้ป่วยตับวายเฉียบพลันที่มีไตวายเฉียบพลันร่วมด้วย

อาภัสณี โสภณสฤษฏ์สุข, บรรยง ภักดีกิจเจริญ, สุรศักดิ์ ลีลาอุดมลิปี, ปิยนุช พูตระกูล, สมชาย เวียงธีรวัฒน์, พัฒนา ศรมยุรา, สุทัศน์ ศรีพจนารถ

ไตวายเฉียบพลันเป็นภาวะแทรกซ้อนที่พบบ่อยในผู้ป่วยโรคตับวายที่รอการผ่าตัดเปลี่ยนตับเนื่องจากระยะเวลาที่รอตับจากผู้บริจาคนานขึ้น ร่วมกับความก้าวหน้าทางการแพทย์ทำให้ผู้ป่วยอาการหนักมีชีวิตรอดมากขึ้น ผู้ศึกษาได้รายงานผู้ป่วยด้วยโรคตับวายและมีภาวะไตวายเฉียบพลันร่วมด้วย ไม่สามารถตรวจพบสาเหตุของตับวายเฉียบพลันในผู้ป่วยรายนี้ ผู้ป่วยได้รับการฟอกไตเป็นเวลา 1 เดือน และรับการผ่าตัดเปลี่ยนตับและปลูกถ่ายไตในเวลาเดียวกันเนื่องจากได้รับการฟอกไตเป็นเวลานาน โอกาสที่ตับวายจะกลับมาทำงานปกติเกิดได้น้อย เมื่อตรวจการทำงานของไตด้วยวิธีทางเวชศาสตร์นิวเคลียร์ที่ 6 เดือนหลังผ่าตัด ไม่พบว่ามีการทำงานของไตคู่เดิม การผ่าตัดเปลี่ยนตับและปลูกถ่ายไตในเวลาเดียวกันจึงอาจมีความจำเป็นในผู้ป่วยตับวายเฉียบพลันที่มีภาวะไตวายเฉียบพลันอยู่เป็นเวลานาน