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Editorial

Hidden pathology of kidney disease after liver transplantation

Liver transplantation is the definite modality for the treatment of end-stage liver disease. Although the surgical approaches have substantially increased the success rate of liver transplantation, there are still a number of obstacles to encounter after liver transplantation. One of them is kidney disease. According to previous reports, liver transplant recipients have a high rate of kidney disease, reaching 80% [1]. The major renal presentation includes acute kidney injury (AKI) and chronic kidney disease (CKD), and both AKI and CKD in liver transplant recipients may lead to end-stage renal disease and increase the risk of cardiovascular disease and mortality. The occurrence of AKI and CKD has remained relatively unchanged despite increased awareness of kidney problems after liver transplantation.

Perioperative problems can affect kidney function in liver transplant recipients. Among them, renal hemodynamic issues are frequently observed during the early period of liver transplantation: surgery-related events, blood losses, hypotension, sepsis, cardiac dysfunction, and volume depletion [2]. It is well known that a decrease in mean arterial pressure (approximately < 70 mmHg) may induce kidney damage. Accordingly, keeping postoperative fluid balance through adequate fluid resuscitation is an important measure for a better early outcome. These hemodynamic issues can be reviewed from the medical records.

It was previously reported that most cases of CKD following liver transplantation were attributable to nephrotoxicity induced by calcineurin inhibitors (CNIs) [3]. CNIs including tacrolimus and cyclosporine may produce afferent and efferent arteriolar vasoconstriction in the kidney, although they have a great effect on graft survival. Alternative immunosuppressive regimens have emerged: mycophenolate mofetil and inhibitors of mammalian target of rapamycin. However, there is insufficient evidence that better or comparable outcomes are achieved by these alternative regimens compared to CNI regimens [4,5]. Accordingly, CNI is currently the backbone of immunosuppressive regimens following liver transplantation. Also, CNI-induced nephrotoxicity should always be considered in the clinical settings where liver transplant recipients have a decreased kidney function.

In the current issue of *Kidney Research and Clinical Practice*, Lee at al investigated histological findings of the kidney from 10 liver transplant recipients with decreased kidney function [9]. The most common diagnosis was glomerulonephritis (GN) such as immunoglobulin A nephropathy ($n=4$), mesangial proliferative GN ($n=1$), focal proliferative GN ($n=1$), and membranous GN ($n=1$). Typical CNI-induced nephrotoxicity was diagnosed in three cases. All of the patients had received CNI regimens.

Although the sample size was small, this study presented some clinical implications. First, the proportion of patients with CNI-induced nephrotoxicity was modest. Rather, GN was the most prevalent cause of kidney disease in that study subset. This finding is not different from the results of other study groups [6–8], in which histology was not limited to CNI-induced nephrotoxicity. The GN may have resulted from the progression of pre-existing GN or new development after liver transplantation. Although the origin of GN is not fully established by these studies, it is important that the management of GN is significantly different from that of CNI-induced nephrotoxicity. In this regard, kidney biopsy may be considered as essential to differentiate the causes of kidney disease in liver transplant recipients. Fortunately, there were no complications after kidney biopsy, although selection bias for indication is unavoidable.

As stated above, a kidney biopsy can reveal a hidden pathology or cause of kidney disease following liver transplantation. However, a kidney biopsy is not essential in all the cases with decreased kidney function because there is no evidence that a kidney biopsy improves the kidney or patient outcomes in liver transplant recipients. Additionally, a successful kidney biopsy, which means that biopsy specimen is properly reviewed and there are no significant complications, cannot be done properly without an experienced practitioner.

In summary, recent studies including the cases described by Lee et al [9] suggest that we need to find causes other than CNI-induced nephrotoxicity in liver transplant recipients with kidney disease. Although some issues hamper the use of a kidney biopsy in routine clinical practice, kidney biopsies for selected patients are required to diagnose and manage the underlying kidney disease properly. Furthermore, kidney biopsies in some patients are warranted to predict the prognosis because liver transplant recipients with kidney disease could have a worse outcome. For these reasons, future studies should address and determine the indication for kidney biopsy in liver transplant recipients.

Conflicts of interest

I do not have any conflict for this manuscript.

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