LETTER TO THE EDITOR

Acute antibody-mediated rejection with graft loss during anti-tuberculosis therapy in kidney transplantation

To the Editor,

Rifampin (RFP) is well-known as a strong inducer of CYP3A4 and can lead to rapid turnover of calcineurin inhibitors (CNIs). Co-prescription of RFP and CNI is a critical issue in kidney transplantation patients [1]. We report a most dramatic case of rapid-onset acute antibody-mediated rejection (AMR) resulting in rapid graft loss within 1 day, occurring during anti-tuberculosis (TB) therapy in a kidney transplant recipient.

A 24-year-old man, diagnosed with immunoglobulin (Ig)A nephropathy in October 2008, underwent peritoneal dialysis in April 2010. He received a live-donor kidney transplant from his mother in March 2011 with regular immunosuppressant agents, including mycophenolate mofetil, tacrolimus, and prednisolone. On November 18, 2014, he came to the emergency room with a chief complaint of exertional dyspnea for 5 days. The initial vital signs and the physical examination were unremarkable. The laboratory data showed a serum creatinine level of 2.34 mg/dL (baseline: 1.8–2.0 mg/dL). Chest X-ray showed cardiomegaly and right-side pleural effusion. TB was proved by pericardial biopsy (Figs. 1A and 1B) and he received anti-TB drugs, consisting of isoniazid 300 mg, RFP 600 mg, ethambutol 1200 mg, and pyrazinamide 1500 mg daily from December 2, 2014. Decreased urine output was noted on the next day and serum creatinine increased to 6.8 mg/dL. Renal biopsy was performed and showed severe acute AMR featuring widespread fibrin thrombosis of the arterioles and glomerular capillaries associated with complete cortical infarction (Fig. 1C–G). Immunofluorescence studies showed negative results for IgG, IgA, IgM, and complement component (C)1q, and only focal weak equivocal C3 staining in the glomerulus. C4d was positive in the peritubular capillaries (Fig. 1H), excluding other morphology mimics, such as thrombotic microangiopathy, disseminated intravascular coagulation, and CNI nephrotoxicity. The morphology mimics either hyperacute rejection or accelerated acute rejection. Hemodialysis treatment commenced. During hospitalization, the dose of tacrolimus started at 6 mg/d, increased to 8 mg/d on December 4 for 1 day, and has remained at 4 mg/d since December 5, 2014 after occurrence of graft loss due to the acute AMR.

Although interaction between RFP and CNIs has been well discussed in the literature, the unique aspect of the current report is that it represents the most dramatic case of rapid-onset acute AMR concurrent with TB and the initiation of therapy. The rapid-onset of acute rejection occurring within 1 day after drug use is unusual. It is possible that both the immune reaction triggered by TB itself and the effect of tacrolimus play an important role in the process. It can also be argued that the rejection was a process in evolution at the time of TB diagnosis; however, his renal function, which was relatively stable before the onset of rejection with creatinine of around 2 mg/dL for several months, is evidence to support that the process was not in progress at the time of TB diagnosis. The limitation of this case report is that the serum tacrolimus level was not closely monitored and the dose was not increased accordingly.

The current case re-emphasizes the importance of prevention and treatment of TB infection in kidney transplantation. To avoid reactivation of latent TB infection after immunosuppressive therapy, diagnosis, and treatment of latent TB are strongly recommended during the pre-transplantation period [1]. To treat active TB infection after transplantation, RFP should be avoided [2], and use of RFP-sparing protocols is highly suggested [3]. Although pre-existing TB is deemed a contraindication to transplantation, several reports have demonstrated that pre-
Pericardial tuberculosis showing necrotizing granuloma (A; H&E stain) with acid-fast bacillus (B; acid-fast stain). Renal biopsy showing severe acute antibody-mediated rejection mimicking hyperacute rejection featuring widespread fibrin thrombosis (D; H&E stain) of the arterioles and glomerular capillaries associated with interstitial hemorrhage (C, white arrow; H&E stain) and neutrophil infiltrate (C, black arrow; H&E stain), with complete cortical infarction (C). Intravascular and intraglomerular thrombosis highlighted by periodic Schiff–methenamine silver stain (E), phosphotungstic acid–hematoxylin fibrin stain (F) and CD61 immunohistochemistry stain indicating the presence of platelets (G). Linear staining of C4d immunoreactivity along inner surface of peritubular capillary, characteristic of antibody-mediated rejection (H). Clinical course during the hospitalization (I). The tacrolimus dose was increased from 6 mg/d initially to 8 mg/d on December 2, 2014 for 1 day, and kept at 4 mg/d from December 5, 2014. H&E = hematoxylin and eosin.
existing TB in patients undergoing transplantation can be managed successfully [4]. If RFP is prescribed, increase in the dose of CNI, and close monitoring of the trough CNI level is essential. The dose of tacrolimus should be increased (even to 2–10 times of the original doses) based on serum levels of tacrolimus in patients receiving RFP therapy [5].

References


