Plasma Terminal Complement Complex Concentrations in Renal Allograft Recipients

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Dear Sir,

The complement system is well known to be one of the important mechanisms to induce tissue damage in several diseases including renal allograft rejection. When the complement cascade is activated by either the classical or the alternative pathway, a terminal complement complex (TCC) consisting of C5b, C6, C7, C8 and C9 (C5b-9) is generated and causes cellular damage. Plasma concentrations of TCC have been used as clinical markers of activity for diseases such as systemic lupus erythematosus [1], acute poststreptococcal glomerulonephritis [2], and membranoproliferative glomerulonephritis [3]. In this study, we examined the plasma TCC concentration in renal allograft recipients, and the results correlated with clinical events such as stable graft function, acute rejection, viral infections and other complications (acute tubular necrosis, cyclosporine A nephrotoxicity, vascular problems).

Twenty patients who received a renal allograft from living related (n = 18) or cadaver (n = 2) donors and 20 healthy subjects were studied. Plasma samples for TCC assay were taken before transplantation and at intervals of 1-2 times per week for 2 months after transplantation, and stored at -70°C until assayed. The concentration of plasma TCC was determined using monoclonal antibodies against a neoantigen of the complex by an enzyme-linked immunosorbent assay [4]. The diagnosis of acute rejection was based on standard clinical grounds (progressive elevation of serum creatinine accompanied by oliguria, fever, or graft tenderness), doppler ultrasonography, or graft biopsy (n = 4).

During the 2-month period 7 acute rejection episodes, 5 viral infections (2 cytomegalovirus, 2 zona zoster and 1 herpes simplex) and 6 other complications (2 acute tubular necrosis, 2 cyclosporine A nephrotoxicity, 1 renal artery stenosis and 1 renal vein thrombosis) were observed. The mean plasma TCC levels are summarized in table 1.

Pretransplant plasma TCC concentrations were not significantly different from those in the control group (p > 0.05). These values remained unchanged after transplantation in patients with stable graft function (p > 0.05). Plasma levels of TCC were significantly higher in patients with acute rejection than in those with stable graft function (p < 0.0001) or other complications (p <

0.01). In patients with viral infections, plasma TCC was also significantly elevated ($p < 0.001$), but graft dysfunction due to other complications did not have a comparable rise in plasma TCC. Although during acute rejection plasma TCC levels were higher than viral infections, the difference did not reach statistical significance ($p > 0.05$). There was no correlation between plasma TCC levels and creatinine levels ($p > 0.05$).

In 6 of 7 acute rejection episodes, significantly raised plasma TCC levels were present within a week before rejection was evident. During this period, the mean plasma TCC level was 4.37 ± 2.5 AU/ml ($p = 0.0001$ vs. stable graft function).

In this study, we found that plasma TCC levels were elevated in renal allograft recipients during acute rejection and viral infections, but not with other complications. However, increments were most pronounced in cases of acute rejection. Therefore, plasma TCC level monitoring may be of benefit in the management of renal allograft recipients.

Table 1. TCC levels in plasma from healthy subjects and renal allograft recipients (mean $\pm$ SD)

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