TRANSPLANTATION

Increased mortality risk in renal transplant recipients with ATG-induced CD4$^+$ T-cell lymphopenia

Prolonged CD4$^+$ T-cell lymphopenia induced by the administration of polyclonal antithymocyte globulins (ATGs) is an independent risk factor for death in renal transplant recipients, according to researchers in France.

Polyclonal ATGs, which cause T-cell depletion, are commonly used in immunosuppressive regimens in transplant recipients. Although T-cell regeneration usually occurs following transplantation, long-term decreases in CD4$^+$ T cells and increases in CD8$^+$ T cells can occur. Didier Ducloux and colleagues had previously found that renal transplant recipients with impaired CD4$^+$ T-cell reconstitution were at increased risk of atherosclerotic events, late opportunistic infections and cancer, but the effect on patient survival was unknown.

In the current study, Ducloux *et al.* analyzed a previously described cohort of 302 stable renal transplant recipients who had undergone transplantation >12 months previously and received ATGs as induction therapy. Mean patient follow-up was 92 months. In total, 36 patients (11.9%) died during follow-up. The mortality rate was higher in patients with persistent CD4$^+$ T-cell lymphopenia (CD4$^+$ T-cell count <300 mm^3) than in patients without this abnormality (24.1% versus 7.6%; $P<0.001$). Cox regression analyses showed that the risk of death was increased almost fivefold in patients with prolonged CD4$^+$ T-cell lymphopenia (adjusted hazard ratio 4.63, 95% CI 1.91–10.65; $P=0.001$).

The researchers also performed a prospective analysis of 100 renal transplant recipients who received ATG induction, to determine whether thymic function at the time of transplantation (assessed as pretransplantation level of T-cell-receptor excision circles [TRECs]) could be used to predict prolonged ATG-induced CD4$^+$ T-cell lymphopenia and transplantation outcomes. Patients were followed for a mean of 74 months. Patients with pretransplantation TREC levels in the lowest tertile were at increased risk of CD4$^+$ T-cell lymphopenia 1 year after transplantation. Higher TREC levels before transplantation were associated with lower rates of death, cancer and infection.

"As pre-transplant thymic function may predict both immune reconstitution and serious post-transplant outcomes after ATG, TREC number should be determined to estimate the benefit-to-risk ratio of such a treatment," states Ducloux.

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Original article Ducloux, D. *et al.* Prolonged CD4 T cell lymphopenia increases morbidity and mortality after renal transplantation. *J. Am. Soc. Nephrol.* **21**, 868–875 (2010)