Immunoprofiling after profound T cell depletion and minimization of immunosuppression in pediatric kidney transplantation: A study of CCTPT/NIAID.

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Despite excellent short-term outcomes for recipients of pediatric kidney transplantation, long-term success is compromised by complications of chronic immunosuppression and chronic allograft nephropathy. We therefore undertook an innovative protocol of minimal maintenance immunosuppression using a steroid-free, calcineurin inhibitor withdrawal protocol at 4 pediatric renal transplant centers. Campath-1H® was used for induction. After 2-3 months of maintenance immunosuppression with MMF and tacrolimus, tacrolimus was withdrawn and replaced with sirolimus. One-year acute rejection rate was 17% and 2 grafts were lost, one due to recurrent FSGS and the other to medication non-adherence. There were no deaths and no cases of PTLD or other serious infections. Twenty-three subjects completed serial assessments of anti-HLA Class I and II antibody by Luminex at 2 years post transplantation. Five subjects (22%) developed new anti-HLA antibody, 1 against Class I, 3 against Class II and 1 against both Class I and II. Antibody development was detected by 12 months in 2 subjects and by 24 months in 3 others. Fifteen subjects had evaluation of lymphocyte recovery for 24 months post transplantation. Peripheral blood mononuclear cells were monitored by flow cytometry and analyzed by FACS Calibur cytometry at 6 times point in the 24 months post transplant. Phenotypes examined in CD4+ and CD8+ T cell subsets included naïve, memory as well as T Regulatory Cells (Tregs). Both naïve and memory CD4+ T cells were profoundly depleted and had not recovered to pre-transplant levels even at 24 months. In contrast, there was significant sparing of memory CD8+ T cells and only a transient depletion of naïve CD8+ T cells which rebounded in 6 months. Percentages of Tregs increased immediately post transplant and remained at least at the level of pre-transplant throughout the 24 months. This pattern of recovery in children resulted overall in an improved Tregs:T effector ratios in pediatric patients. Taken together with Tregs sparing, these observations suggest that this protocol could permit less maintenance immunosuppression in children. This protocol is now being extended to reduce immunosuppression to monotherapy.