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Increased Circulating T lymphocytes Expressing HLA-DR in Kidney Transplant Recipients with Microcirculation Inflammation

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Background: The goal of this study was to compare the histological grading of renal allografts, according to the Banff scoring scheme, with the activity of circulating T lymphocyte subsets and HLA-DR positive monocytes in kidney transplant recipients (KTRs).

Methods: In this study, we included 24 KTRs with acute renal allograft dysfunction who underwent indication biopsy. Flow cytometry was used to estimate the frequencies of serum HLA-DR$^+$, CD4$^+$, CD8$^+$, and CD25$^+$ T lymphocytes and HLA-DR-positive monocytes obtained at the time of biopsy. The sum of the scores of g + ptc, i + t, ci + ct, and cv + ah was used to assign a histological grade to the renal allograft samples, according to the Banff 2013 classification scheme.

Results: The frequencies of CD4$^+$HLA-DR$^+$/CD4$^+$ T cells and CD8$^+$HLA-DR$^+$/CD8$^+$ T cells were significantly increased in KTRs with a microcirculation inflammation (MI) sum score $\geq$ 1 when compared with KTRs with an MI sum score = 0. Between these two T cell subsets, CD4$^+$HLA-DR$^+$/CD4$^+$ T cells were positively correlated with the MI sum score. However, no significant differences were observed between the two groups categorized based on the sum of scores of i + t, ci + ct, and cv + ah. Analysis using the receiver operating characteristic curve showed that antibody-mediated rejection could be predicted with a sensitivity of 80.0% and a specificity of 94.7%, using a cutoff value of 29.6% frequency of CD4$^+$HLA-DR$^+$/CD4$^+$ T cells.

Conclusion: In KTRs, MI was significantly associated with an increased frequency of activated T lymphocytes expressing HLA-DR. Further large-scale studies are needed to confirm the utility of circulating CD4$^+$HLA-DR$^+$/CD4$^+$ T cells as a noninvasive, immunologic monitoring tool for the prediction of antibody-mediated rejection.

Keywords: antibody-mediated rejection, kidney transplantation, Microcirculation inflammation, T-lymphocyte