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Clinical usefulness of lymphocyte subset analysis for the prediction of acute rejection in kidney transplant recipients

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Objectives : Previous studies have shown that lymphocyte subset analysis is useful in predicting the clinical status of kidney transplant recipients (KTRs). In this study, we performed a multi-color flow cytometry to investigate T cell and B cell subset proportions in KTRs with acute rejection (antibody mediated rejection and T cell mediated rejection) in comparison to KTRs with different clinical or pathologic situations.

Methods : At first, we included 48 KTRs from three transplant centers and isolated PBMC from samples taken at the time of allograft biopsy. These were then divided into 3 groups according to pathologic diagnosis; the Normal biopsy control (NC) (n=13) group, Acute rejection (AR) (n=30) group, and the Calcineurin inhibitor toxicity (CNIT) (n=5) group. We performed a multi-color flow cytometry analysis using the following platforms: CD4+ (PE-cy7) CCR4+(PE) CCR6+(APC), CD4+ (PE-cy7) CCR7+(APC) CD45RA+ (FITC), CD8+ (APC) CCR7+ (streptavidin cy5.5) CD45RA+ (FITC), CD4+ (PE-cy7) CD28null (PE) CCR6+ (APC), CD4+ (PE-cy7)CD28null (PE) CD57+ (FITC) CD161+(APC), CD8+ (APC) CD28null (PE) CD57+(FITC), CD4+ (PE-cy7) CD25high (APC) CD127low (FITC), and CD19+(FITC) CD24+ (PE) CD38+ (Percp cy5.5). We compared the proportion of each immune cell subset among the 3 groups. We validated our results using another independent cohort (n=45) (NC=20, AR=16, CNIT=9) based on the primary results.

Results : Out of various T cell and B cell subsets, the percentage of CCR7+CD8+ T cells was significantly decreased in the AR group compared to the NC group ($P<0.05$). In contrast, the percentage of CD28nullCD57+ T cells, CCR7-CD45RA+/CD8+ T cells and CCR4+CCR6+/CD4+ T cells showed increase in the AR group compared to the NC or CNIT group. In the validation study using the independent cohort, percentage of CCR7+CD8+ T cells were

decreased in the AR group and CD28nullCD57+ T cells, and CCR7-CD45RA+/CD8+ T cells were significantly increased as well. However, CCR4+CCR6+/CD4+ T cells failed to show significant difference in the AR group in comparison to the other clinical groups. When we calculated the ratio of CCR7+CD8+ T cells and CD28nullCD57+ CD8+ T cells, it showed significant value for the prediction of AR in the whole clinical cohort (AUC=0.679, P=0.02).

Conclusions : This study suggests that combined monitoring of the ratio between CCR7+ and CD28nullCD57+ T out of CD8+ T gating may be useful for the prediction of AR. Validation of this result in a prospective cohort may be required.

Keywords : Acute rejection, kidney transplantation, flow cytometry, T cells, B cells