Identification of peripheral CD154+ T-cells and HLA-DRB1 as biomarkers of acute cellular rejection in adult liver transplant recipients

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Abstract

Decreasing graft rejection and increasing graft and patient survival are great challenges facing liver transplantation (LT). Different T-cell subsets participates in the acute cellular rejection (ACR) of the allograft. Cell-mediated immunity markers of the recipient could help to understand the mechanisms underlying acute rejection. This study aimed to analyse CD4+CD154+ and CD8+CD154+ T-cells in a cohort of adult liver patients undergoing LT to determine the influence on ACR using multiparametric flow cytometry functional assay. Thiry patients were immunologically monitored at baseline and during 1 year post-transplant. Two groups were established, with (ACR) and without (NACR) acute cellular rejection. Leukocyte, total lymphocyte, percentages of CD4+CD154+ and CD8+CD154+ T-cells, HLA mismatch between recipient-donor and their relation with ACR as well as the acute rejection frequencies were analysed. T-cells were stimulated with concanavalin A (Con-A) and surface antigens were analysed by FACS analysis. A high percentage of CD4+CD154+ T-cells (p=0.001) and a low percentage of CD8+CD154+ T-cells (p=0.002) at baseline were statistically significant in ACR. A receiver operating characteristic analysis determined the cut-off values capable to stratify patients at high risk of ACR with high sensitivity and specificity for CD4+CD154+ (p=0.001) and CD8+CD154+ T-cells (p=0.002). In logistic regression analysis, CD4+CD154+, CD8+CD154+ and HLA mismatch were confirmed as independent risk factors to ACR. Post-transplant percentages of both T-cell subsets were significantly higher in ACR, despite variations compare to pre-transplant. These findings support the selection of candidates for LT based on the pre-transplant percentages of CD4+CD154+ and CD8+CD154+ T-cells in parallel with other transplant factors

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