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The significance of non-HLA autoantibodies as a biomarker of chronic lung allograft dysfunction in lung transplantation

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Introduction: Lung transplantation generally shows poor outcomes compared to other solid organ transplantations. Chronic lung allograft dysfunction (CLAD) is the most crucial factor related to such dismal outcomes. While the role of non-HLA antibodies in kidney or liver transplantation is well established, little is known in Lung transplantation. This study aims to evaluate the role of non-HLA autoantibodies in the prediction of CLAD in Lung transplantation recipients.

Methods: Among 58 patients who received Lung transplantation at Samsung Medical Center from 2016 to 2021, 44 sera from 22 patients who survived more than one year after Lung transplantation were included in the exploration study using Luminex bead array tests detecting 39 non-HLA autoantibodies and anti-angiotensin type 1 receptor (AT1R) antibody ELISA test. Further verification study, sera of non-CLAD patients and CLAD patients from the Korean Organ Transplantation Registry (KOTRY) were subjected to single ELISA for selected target autoantibodies.

Results: Among 22 patients who survived more than a year after the first Lung transplantation, there were 18 non-CLAD and 4 CLAD patients according to the latest ISHLT CLAD definition. In the exploration study, three autoantibodies were significant as predictors of CLAD; pre-transplant PLA2R (P=0.013), post-transplant IFIH1 (MDA-5) (P=0.01), and post-transplant TNFA (P=0.01). AT1R and Tubulin antibodies were not significant in either pre-transplant or post-transplant sera in the exploration study. To confirm the association between candidate autoantibodies and CLAD, confirmative ELISA tests with a larger number of sera are on the way.

Conclusion: The presence of non-HLA autoantibodies in the pre- and post- transplant period might serve as promising biomarkers of CLAD, however, further studies with large prospective cohort would be warranted for the practical application of each biomarker.