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COVID-19 Vaccine Triggered Rejection in Lung Transplant Recipients: A Case Series

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Purpose: Anti-severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) vaccination is recommended by AST, ISHLT, and CDC in all transplant recipients. Lung transplant recipients (LTR) are at a higher risk of developing severe symptoms due to higher immunosuppression (IS) and baseline compromised graft function. Limited antibody response to messenger RNA (mRNA) vaccines has been reported in LTR, with the majority mounting a response after the 2nd dose. In this series, 3 patients developed new and significant respiratory compromise after their 2nd vaccine dose consistent with antibody mediated rejection (AMR). To our knowledge, this is the first published case series of vaccine induced rejection in LTR.
Methods: Retrospective chart review of our cohort showed 46% fully vaccinated and an additional 2.5% partially vaccinated patients. Three fully vaccinated patients with approved mRNA vaccines (2 Moderna, 1 Pfizer-BioNTech) were identified after developing severe respiratory compromise post 2nd vaccine dose. Evaluation revealed AMR as the underlying etiology.
Results: All patients were female, ages 50-70 years old, between 6 months and 2 years post-transplant. No previous rejection episodes. All were on standard IS as per institution protocols. Two were hospitalized with hypoxic respiratory failure within 2 weeks of their 2nd vaccine dose. The 3rd was seen at clinic for milder similar symptoms, later progressing and requiring supplemental oxygen (O2) and hospitalization. Imaging showed new lung infiltrates, infectious work up was negative. Biopsies did not show any cellular rejection. All developed new DSAs and received treatment for AMR with plasmapheresis, IVIg, and Rituximab. Two recovered their lung function and are off supplemental O2, the 3rd did not and is relisted for transplant.
Conclusion: While LTR have a diminished response to SARS-CoV-2 vaccines making them more vulnerable to the disease, their immune system's response may not always be clear. We report three cases of patients developing severe AMR from new DSAs that appear to be triggered by the COVID-19 vaccine. This vaccine responses should be collected in a database where each case can be investigated to help better understand the mechanism behind them and hopefully identifying LTR at risk. This can then be used to modify vaccination strategies and aid in preventing adverse outcomes in this vulnerable group of patients.

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First Report of Daratumumab in Clinical Lung Transplantation

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Purpose: Antibody mediated rejection (AMR) after lung transplantation is difficult to treat and often results in death or graft loss. Therapies targeting antibodies or B cells are in many cases inadequate for decreasing donor specific antibodies (DSA), particularly when they are directed against MHC class II. Daratumumab (DAR) is a humanized anti-CD38 monoclonal antibody, which induces plasma cell death through multiple mechanisms including complement- dependent cytotoxicity, antibody-dependent phagocytosis, and apoptosis. Based on these properties it may have the potential to reduce the amount of DSAs and therefore improve outcome after AMR.
Methods: Retrospective analysis of all patients who received daratumumab as an add on rescue therapy for AMR or for desensitization pre/post-transplant at our center.
Results: Six patients received daratumumab due to the following reasons: 5 patients with de novo DSAs and AMR, 1 patient with pre-transplant DSAs and post-transplant immunadsorption without clinical AMR. Daratumumab was safely administered with just mild infusion reactions and no severe adverse event. Of not, none of the patients developed and infectious complication. Five of the 6 patients showed a significant decrease of their DSAs with a reduction of MFI values after 6-8 weeks to <50% of the baseline . Despite this early success, four patients developed CLAD (,two of which required retransplantation. The remaining two patients stabilized with their lung function and did not develop CLAD.
Conclusion: Treatment for AMR remains challenging, especially in the presence of class II HLA antibodies. Daratumumab might be a promising addition to the AMR treatment panel, prospective clinical studies are needed.

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The Normalised Acute Rejection Score in the First Year Post Transplant and Its Association with CLAD

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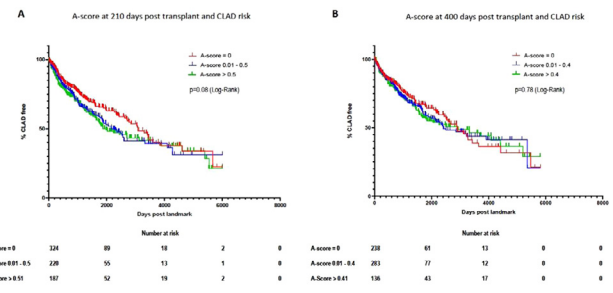
Purpose: The Acute Rejection Score (A-score) is a measure of the burden of acute cellular rejection (ACR) over time in lung transplant (Ltx) recipients which is often incorporated into multivariate analyses assessing LTx outcomes. We aim to assess the correlation between A-score at 6 and 12 months post Ltx and chronic lung allograft dysfunction (CLAD).
Methods: We performed a retrospective cohort analysis on adult 1st double LTx recipients from January 2003 to March 2018, with minimum 6 months of follow-up and 1 or more evaluable transbronchial biopsies (TBBX) in the 1st year post Ltx. A-score was calculated at 6 months (approximated as 210 days) and 1 year (400 days) post-LTx as the sum of all ACR histologic A-grades, divided by the number of TBBX up to that time point. AX grade biopsies were excluded from the calculation. CLAD was determined according to 2019 ISHLT guidelines. Kaplan-Meier curves were compared using the Log-Rank test.
Results: Of 828 1st double lung transplants, 31 were excluded with less than 6 months of follow-up and 23 had no evaluable biopsies in the first year post Ltx (final n=774). Mean follow-up was 2102 days to graft failure (death or retransplant) or last available pulmonary function test. 345 patients (45%) developed CLAD. Mean A-score was 0.37 and 0.32 at 210 and 400 days, respectively; median non-zero A-score was 0.5 and 0.4. Kaplan-Meier curves comparing A-score 0 with scores above and below the median were not significantly different (p=0.08 and 0.78 for 210 and 400 days) (Figure A,B). Log-rank comparison of only non-zero groups was not significant (p=0.78 and 0.93 at 210 and 400 days).
Conclusion: A-score at 210 and 400 days post Ltx, when setting a cutoff at the median, is not significantly associated with CLAD. Further study with Cox proportional hazard modelling of the A-score as a continuous and time-dependent variable will be conducted to assess the impact on the risk of CLAD.



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Unilateral vs Bilateral Lower Lobe Surveillance Transbronchial Biopsies in Patients with Bilateral Lung Transplant Patients

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