VAC_07 - Cellular response in severe adverse events after COVID-19 vaccination

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Introduction: Vaccination is the most effective prevention against SARS-CoV-2 infection and COVID-19 vaccines meet strict safety requirements. Although, severe adverse events (SAE) following COVID-19 vaccination were reported, such as Vaccine-induced immune thrombotic thrombocytopenia (VITT), Guillain- Barré syndrome (GBS) and others. Pharmacovigilance studies are important to ensure vaccine safety and reduce the negative impact of vaccine hesitancy on immunization programs.

Objectives: To understand the underlying mechanisms of SAE following COVID-19 vaccination by analyzing the immunologic profile of vaccinated individuals.

Methodology: Peripheral blood mononuclear cells (PBMC) were isolated from 32 SAE cases (CAAE: 58916622.0.0000.5262), comprising VITT (n=14), SBG (n=13), myelitis (n=3), ADEM (n=2) pathologies. PBMC responses were stimulated for 16 hours using a mix of peptides from SARS-CoV-2 Spike glycoprotein. Seven healthy vaccinated individuals were included as controls. A flow cytometry panel was used to characterize PBMC subpopulations, including lymphocytes and NK cells, from cases and controls and Kruskal-Wallis and Dunn's tests were performed ($p<0.05$). Furthermore, inflammatory markers were quantified in stimulated PBMC supernatant from cases and compared to controls using non-parametric unpaired t-test ($p<0.05$).

Results: A lower frequency of activated CD8+T cells (CD3+CD8+CD38+) was found in cases of SAE (1.15%) when compared to healthy individuals (5.78%), while no changes in the percentage of activated CD4+T cells (CD3+CD4+CD38+), activated monocytes (CD14+HLADR+), and NK cells (CD56+) were observed between the two groups. In a more accurate analysis, the SAE group was stratified by clinical outcome (VITT and SBG) and a lower percentage of NK cells was seen in the VITT group but not in the GBS group. Moreover, a lower concentration of IL-4, IL-6, IL-7 and GM-CSF was detected in the supernatant of PBMCs from SAE cases.

Conclusion: Our findings indicate that individuals with SAE exhibited a decreased functional response of CD8+T lymphocytes which are crucial for the antiviral cellular response. This immunophenotypic pattern suggests a reduced production of cytokines associated with the cellular response. As a perspective, we intend to evaluate through RNAseq the correlation between immunodeficiency and the occurrence of SAE.

Keywords: Severe adverse events; COVID-19 vaccine; Activated CD8+T