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Lung recovery after COVID-19 pneumonia: immunological insights of PD-1 T cells

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Background
Immune system plays a significant role in the pathogenesis of COVID-19 severity. However, the factors remaining prolonged lung recovery are still barely understood. Immune checkpoint molecules as Programmed death-1 (PD-1) and ligand PD-L1 are associated with COVID-19 severity and prognosis. The aim of this study was to analyze the relationship between blood PD-1 CD4+ and CD8+ T cells and the radiological lung abnormalities at the post-COVID period.

Methods
Peripheral blood samples were collected from post-COVID pneumonia patients at three visits: 3, 6 and 12 months after the discharge from hospital. The analysis of CD4+PD-1 and CD8+PD-1 T-cells was performed using flow-cytometry and analyzed by the experienced immunologist.

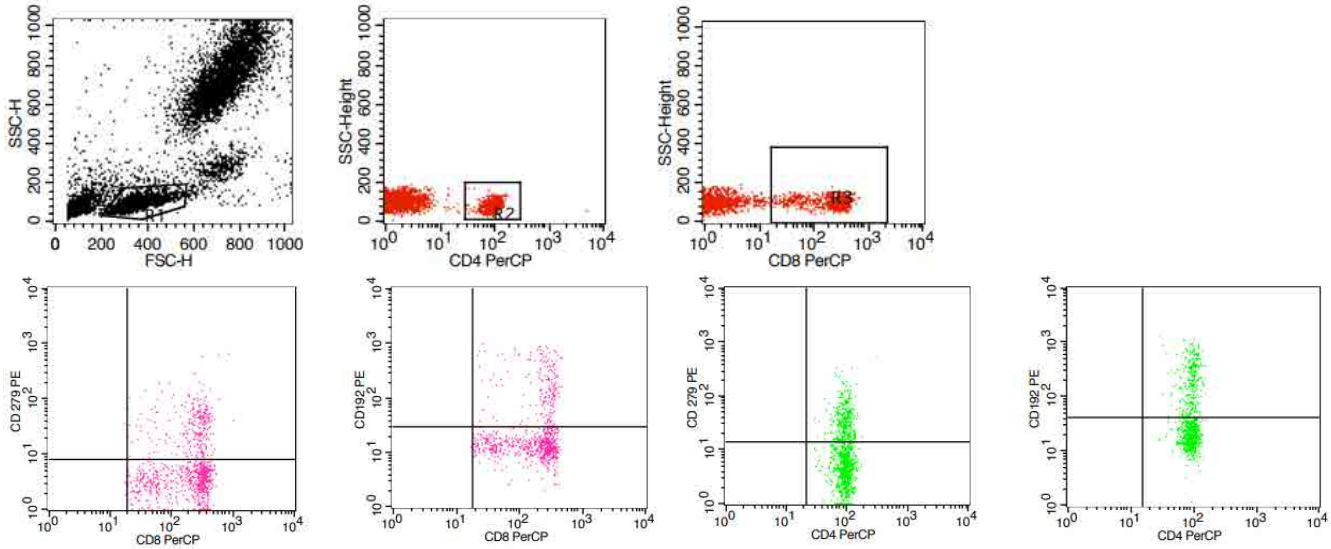

Figure 1. Fig. A: Flow cytometry analysis of peripheral blood T lymphocytes. CD4+ and CD8+ T cell subsets are determined within lymphogate; Fig. B: PD1 (CD279) and CCR2 (CD192) expression on CD4+ T cells; Fig. C: PD1 and CCR2 expression on CD8+ T cells.

Chest CT-scan was also performed; and total radiological score (RS) by radiologists were evaluated - reticular and possible pro-fibrotic lung changes and "ground glass opacity" taking into account.
For the detailed analysis, the patients were divided into 2 groups - moderate and severe COVID-19 survivors, - based on WHO criteria.

Results
Forty-seven patients (mean age 57,8, SD±9,1) were included (24 male, 23 female). Nineteen patients were after moderate and 28 after severe COVID-19 disease. There was no significant difference between disease severity groups according to the age and sex.
Higher CD4+PD-1 than CD8+PD-1 T lymphocyte counts were observed at all 3 visits, and this trend remained unchanged by the total number of patients at each visit. No statistically significant difference was observed when comparing the COVID-19 severity groups, and no difference was observed when comparing changes in PD-1 T cell subtypes over time.
Radiological scores were significantly higher in the severe disease group and decreased over time ($p < 0.001$).

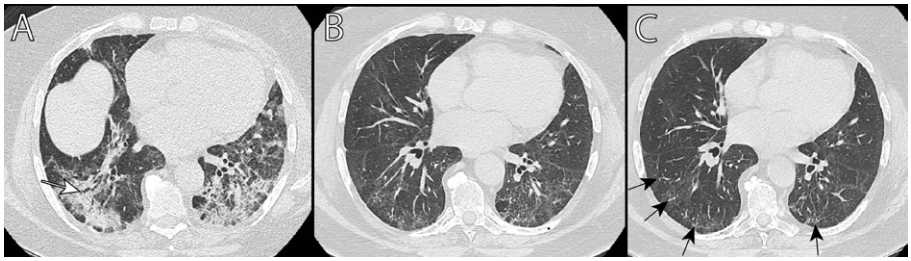

Figure 2. (A) CT at initial COVID-19 presentation. Bilateral multifocal organizing consolidations with bronchiectasis (white arrow) and surrounding ground glass opacities. (B) 3 month follow-up CT. (C) CT obtained after 6 months. Almost complete resorption of ground glass opacities with persisting subpleural curvilinear parenchymal bands (black arrows)

There was no significant association between peripheral blood CD4+ and CD8+ PD-1 T cells and disease severity, neither in radiological scores nor in the decrease over time.

Conclusion
No significant association on peripheral blood CD4+ and CD8+ PD-1 T cells was found with radiological scores ether with disease severity, nor with radiological lung pathological changes within the lung recovery period in COVID-19 pneumonia survivors. More studies are needed to confirm this hypothesis. But we found significant lung structure recovery over time, which is consistent with literature data.