Comparison of Immune Responses Through Multiparametric T cell Cytokine Expression Profile Between Children With Convalescent COVID-19 Or Multisystem Inflammatory Syndrome

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Abstract

The immunological pathways that cause Multisystem Inflammatory Syndrome after SARS-CoV-2 infection in children (MIS-C) remain under investigation. The aim of this study was to prospectively compare the T-cell cytokine expression profile between children with convalescent COVID-19 or MIS-C. Peripheral blood mononuclear cells (PBMCs) were isolated from unvaccinated children with acute MIS-C (MIS-C_A) before immunosuppression, convalescent MIS-C (one month after syndrome onset, MIS-C_C), convalescent COVID-19 (one month after hospitalization) and healthy, unvaccinated controls. Intracellular expression of IL-4, IL-2, IL-17, IFN-γ, TNF-α and Granzyme B, post SARS-CoV-2-Spike antigenic mix stimulation of T cell subsets was analyzed by 13-colour Flow Cytometry. Twenty children (4 MIS-C_A, 4 MIS-C_C, 8 post-COVID-19, and 4 controls) with median age (IQR): 11.5(7.25-14) years were included in the study. From the comparison of the flow cytometry analysis of the 14 markers of MIS-C_A with the other 3 groups (MIS-C_C, post-COVID-19 and controls), statistically significant differences were identified for: 1. CD4 $^{+}$IL-17 $^{+}$/million CD3 $^{+}$: 293.0 (256.4-870.9) vs 50.7 (8.4-140.5); *P*-value:0.03, vs 96.7 (89.2-135.4); *P*-value:0.03 and vs 8.7 (0.0-82.4); *P*-value:0.03, respectively, 2. CD8 $^{+}$IL-17 $^{+}$/million CD3 $^{+}$: 335.2 (225.8-429.9) vs 78.0 (31.9-128.9) vs 84.1(0.0-204.6) vs 33.2 (0.0-114.6); *P*-value:0.05, respectively 3. CD8 $^{+}$IFN-γ $^{+}$/million CD3 $^{+}$: 162.2 (91.6-273.4) vs 41.5 (0.0-77.4); *P*-value:0.03 vs 30.3(0.0-92.8); *P*-value:0.08, respectively. In children presenting with MIS-C one month after COVID-19 infection, T cells were found to be polarized towards IL-17 and IFN-γ production compared to those with uncomplicated convalescent COVID-19, a finding that could provide possible immunological biomarkers for MIS-C detection.

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