

Unraveling T-Cell Dysregulation In Chronic Nonbacterial Osteomyelitis

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Introduction

Chronic nonbacterial osteomyelitis (CNO) is a poorly understood autoinflammatory disease characterized by an altered innate immune system resulting in cytokine dysbalance. Despite its clinical impact, validated biomarkers remain unavailable. Emerging evidence links alterations in circulating lymphocyte subpopulations to SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis) syndrome, which shows similarities to CNO in adulthood.

Objectives

This study aimed to evaluate differences in circulating lymphocyte subpopulations in pediatric CNO compared to juvenile idiopathic arthritis (JIA) and healthy controls (HC), expanding upon immunophenotypic insights from SAPHO syndrome.

Methods

History and clinical data of CNO patients were collected, and cytometry of lymphocyte subpopulations was performed using an established immunophenotyping panel. Comparative analyses of B, T, and NK (natural killer) cell subpopulations were conducted across groups. Statistical analysis was performed using the nonparametric paired Wilcoxon-test, with $p < 0,05$ considered statistically significant.

Results

A total of 16 CNO patients were analyzed alongside age- and sex-matched JIA patients and HC. Results revealed reduced CD56+CD16+ NK cells in CNO patients compared to HC. Additionally, increased effector memory RA+ (EMRA) T-cells and increased exhausted helper T cells were observed in CNO relative to HC but not in comparison to JIA. Furthermore, regulatory T-cells (T_{reg}), including total and naïve subsets (helper and cytotoxic Treg), were elevated in CNO compared to HC but not when compared to JIA. These findings are shown as boxplots in figure 1.

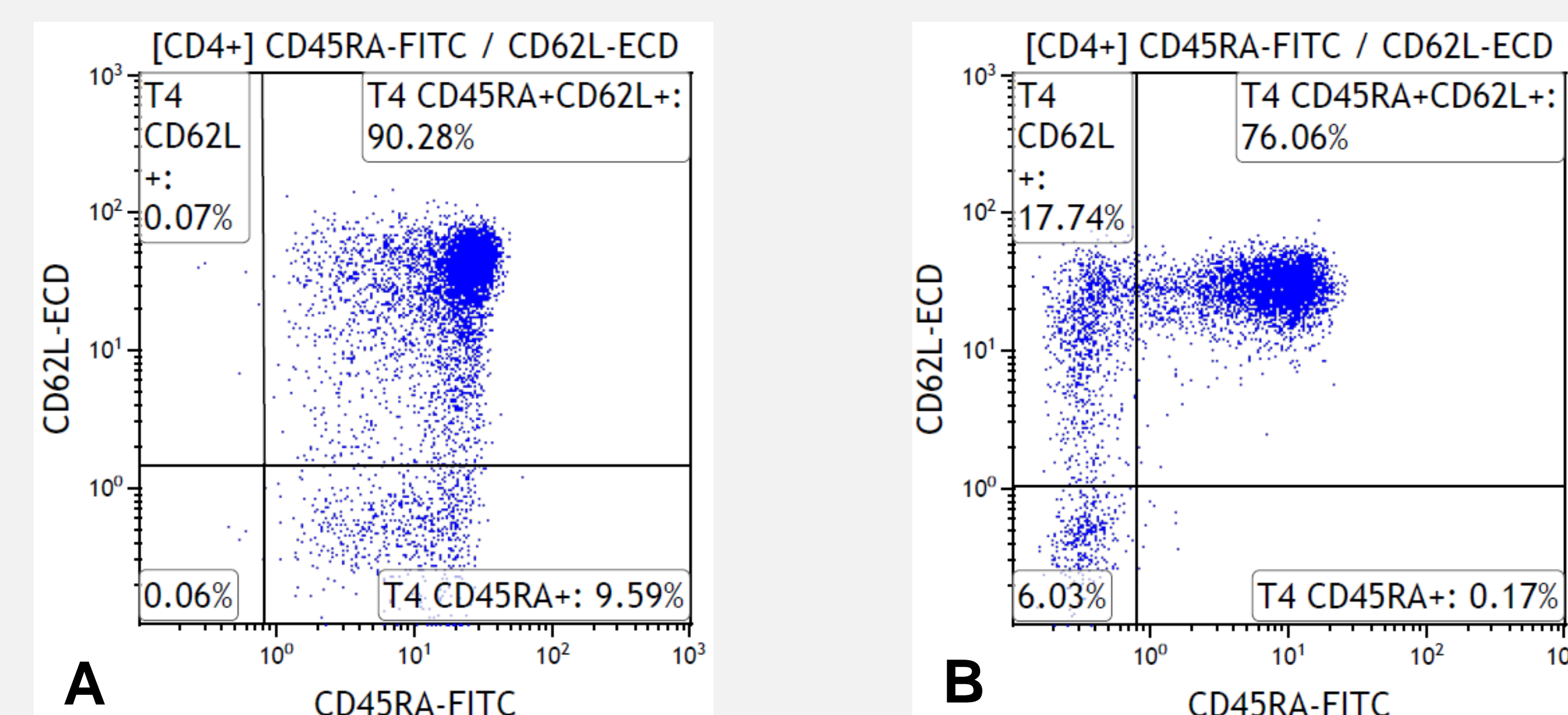


Figure 2: flow cytometry of CD4+ EMRA T-cells of CNO (A) and HC (B)

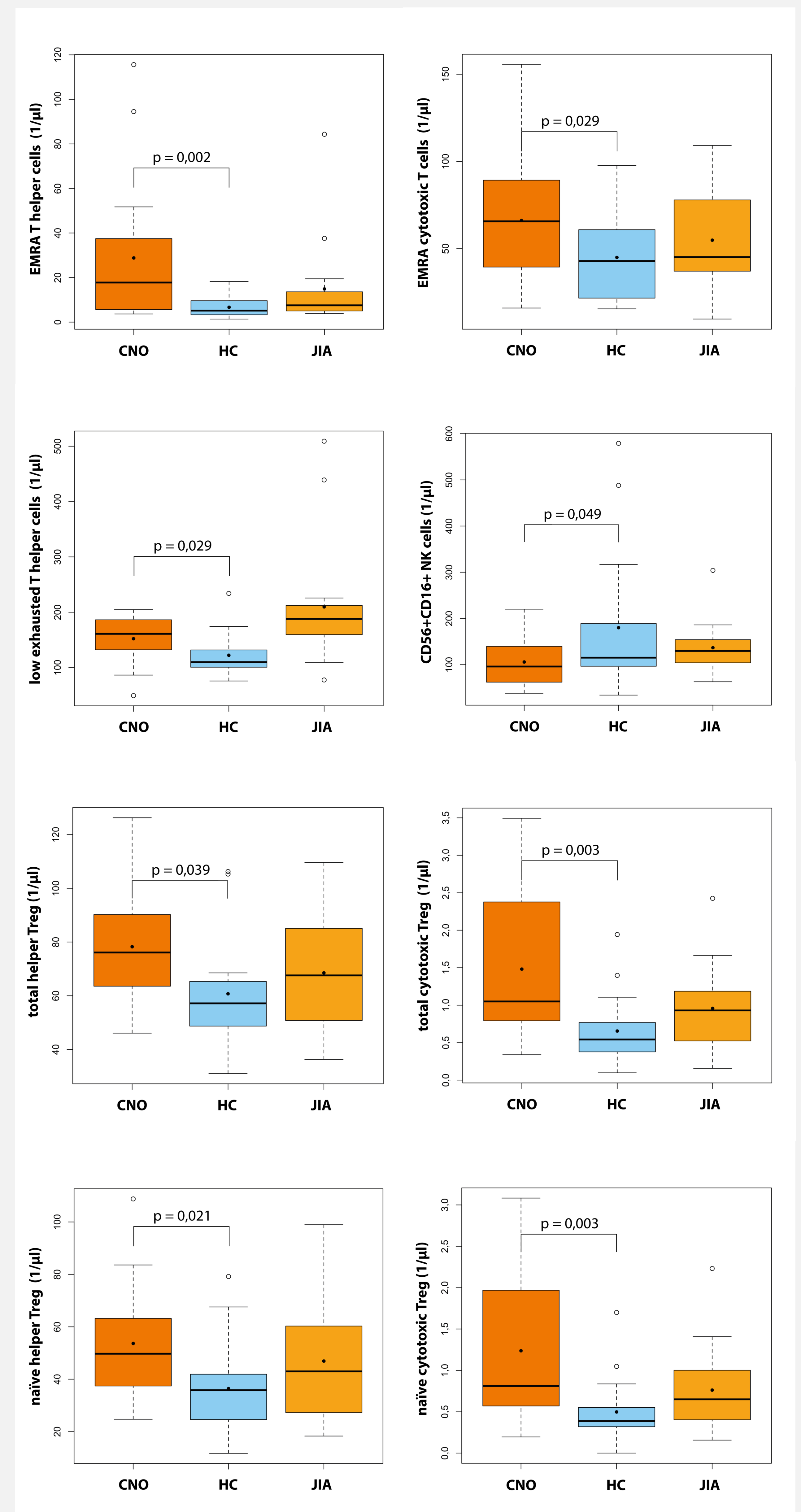


Figure 1: Boxplots represent results of EMRA T cells, low exhausted helper T cells, CD56+CD16+ NK cells and Treg with subsets (with upper and lower quartile) of CNO, HC and JIA with p-values. The median is marked as horizontal line, the mean as dot.

Conclusion

Distinct alterations in lymphocyte subpopulations, including changes in NK and T-cell subsets, suggest potential roles for T-cell senescence and exhaustion in CNO pathophysiology. These findings hint at autoimmune mechanisms and potential therapeutic targets but may also represent secondary effects, given the similarities with JIA. The elevation of T_{regs} in the CNO group compared to HC was unexpected and may reflect the heterogeneity of the CNO cohort. Further research is required to elucidate these pathways and validate therapeutic implications.