

Abstract Type : Oral

Abstract Submission No. : OR-1430

IL-17/IFN- γ double positive Th17 cells selectively express P-gp and are refractory to glucocorticoids in nephrotic syndrome patients

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Objectives: Th17 cells and cytokine interleukin (IL)-17 are involved in many autoimmune diseases. Recently, IL-17/interferon IFN- γ double-positive Th17 cells were found to be allied with inflammatory diseases. P-glycoprotein (P-gp) on lymphocyte effluxes out steroid and prevents its action. We planned to study the frequency of P-gp expressing IL-17/IFN- γ double positive Th17 cells in steroid-sensitive nephrotic syndrome (SSNS) and steroid-resistant nephrotic syndrome (SRNS) patients.

Methods: We analysed the frequency of pathogenic IL17/IFN- γ double-positive Th17 lymphocytes and P-gp expression on their surface by flow cytometry in SSNS (n = 32; mean age: 9.06 ± 5.84) and SRNS (n = 28; mean age: 11.29 ± 3.73) patients. We also included 15 age and sex matched healthy controls. All patients were of biopsy proven minimal change disease and all patients were treated with steroids. All patients were recruited as per the criteria of ISKDC.

Results: We found a significant increase in the frequency of CD4+IFN- γ +Th1 (P = 0.01), CD4+IL-17+Th17 (P = 0.006), and CD4+ IFN- γ + IL-17+Th17 (P < 0.001) cells in SRNS as compared to SSNS patients and healthy controls (P < 0.001). Of the Th1, Th17, and IL-17/IFN- γ double positive Th17 cells, 72.37%, 78.45% and 95.8% cells were expressed P-gp on their surface in SRNS; however, 45.0%, 30.27%, and 30.1% cells expressed P-gp in SSNS group and 30.99%, 15.51%, and 15.62% in healthy controls, respectively. We also observed that P-gp expression correlate positively with Th17, (r= -0.507, p= 0.003) and IL-17/IFN- γ double positive Th17, (r= 0.739, p< 0.001) lymphocytes significantly. However, there was no association between P-gp expression and Th1 cells.

Conclusions: Higher frequency of IL-17/IFN- γ double positive Th17 cells with high P-gp expression may be associated with steroid resistance in nephrotic syndrome patients.