Background: ALPS is a rare disorder due to a defective apoptotic mechanism leading to abnormal lymphoproliferation and autoimmunity. The disease is difficult to identify in the early phase when it may be misdiagnosed. Elevated TCR alpha-beta CD4-CD8- lymphocytes (double negative T lymphocytes DNT) together with hyperIgG, high levels of IL10, IL18, vitamin B12 and soluble Fas ligand have been suggested as the main ALPS hallmarks (1). Therefore, a specific flow cytometry panel (DNT cells, ratio of CD25+CD3+, HLA−DR+CD3+ cells, B220+ T-cells, and decreased CD27+ memory B cells) has been proposed to serve as a diagnostic screen for ALPS (2).

Objectives: To evaluate the usefulness of a specific lymphocyte flow cytometry panel in the early identification of ALPS/ALPS-like disorders in a cohort of patients with undifferentiated autoinflammatory or autoimmune disorders.

Methods: The clinical data of patients referred to the pediatric Rheumatology Unit of the Istituto Giannina Gaslini Hospital for a suspicion of autoimmune or autoinflammatory condition from October 2015 to April 2018, were retrospectively analyzed. Data on clinical manifestations, laboratory workup, genetic analysis and treatment were collected. Flow cytometry was included among the screening panel: DNT, CD25+CD3+, HLA−DR+CD3+ cells, B220+ T-cells, and CD27+ memory B cells. The use of the specific flow cytometry panel, comprehensive of the ALPS hallmark, has been proposed to serve as a diagnostic screen for ALPS.

Results: Of 475 patients were retrospectively analyzed, 211 patients not fulfilling the inclusion criteria were excluded. The patients were classified as follows: i) Autoimmune disease 26 pts (10 SLE; 3 MCTD; 6 JM; 5 Behçet; 1 Sj; 1 Kawasaki) ii) Juvenile Idiopathic Arthritis 35 pts iii) Monogenic systemic autoinflammatory disease (MSaID) 27 pts (17 FMF; 3 MKD; 1 TRAPS; 4 DADA2; 2 SAVI) iv) PFAPA 100 pts v) Systemic Undetermined Recurrent Fever 45 pts vi) Undetermined-SaID 15 pts vii) ALPS/ALPS probable 16 pts. The flow cytometry panel showed, as expected, an elevation of DNT in all ALPS patients. Among the other parameters, CD3CD25+/CD3HLADR+, and B220+ T cells, were significantly altered in 75% of ALPS patients. Conversely, B CD27+ did not differentiate ALPS from the other subgroups. The multivariate analysis revealed 5 clinical/laboratory parameters that showed the higher independent association to ALPS in the cohort of patients. Spleenomegaly, female gender, elevated DNT, arthalgia and elevated alfabetα+B220+ lymphocytes were positively and significantly associated to ALPS.

Conclusion: The use of the specific flow cytometry panel, comprehensive of DNT, B220+, HLA-DR and CD25, in patients with undifferentiated autoinflammatory or autoimmune disorders may identify a subgroup of patients with ALPS.

References:

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