CD4+CD25HIGHFOXP3+ REGULATORY T CELLS IN THE COURSE OF ATOPIC DISEASES IN CHILDREN

Anna Stelmaszczyk-Emmel[1], Anna Zawadzka-Krajewska[2], Agnieszka Szypowska[3], Anna Podsiadłowska[1], Marek Kulus[2], Urszula Demkow[1]

[1]Department of Laboratory Diagnostics and Clinical Immunology of Developmental Age, [2] Department of Pediatric Pneumonology and Allergology,and [3]Department of Paediatrics Medical University of Warsaw, Poland

Atopic allergy is among immune tolerance-related disorders resulting from a failure of regulatory network. Regulatory T cells (Tregs) play a leading role in the development of the homeostasis in immune system by limiting inflammatory responses and promoting immune tolerance. The aim of the study was to determine the role of Tregs in the pathogenesis of atopic diseases in children by exploring the relationship between Tregs frequency and activation markers and the clinical manifestations of the disease as well as serum specific IgE (sIgE) level. 20 allergic and 50 healthy children were enrolled to the study. PBMCs were stained with monoclonal antibodies (anti-CD25, -CD4, -CD127, -FoxP3, -CD69, -CD71) and evaluated using flow cytometry. Tregs in peripheral blood were identified as CD4+CD25+^{high}FoxP3+CD127- T cells. The percentage of Tregs in allergic patients (2.3%) was significantly decreased in comparison to healthy controls (4.6%) (p=0.003). The frequency of Tregs in patients with symptoms of AD (atopic dermatitis) and/or FA (food allergy) (1.7%) was significantly lower than in allergic patients without AD and/or FA symptoms (2.9%) (p=0.04). In the subgroup of patients allergic to birch pollen sIgE serum concentrations to birch allergen was correlated with the relative number of Tregs. A significant correlation between Tregs percentage and sIgE serum concentration (r=-0.47, p=0.036) was found. The percentages of Tregs did not differ between subgroups of patients sensitized to few (1-2) and to multiple antigens (3 and more). Relative fluorescence intensities (RFI) of FoxP3 expression were also compared between patients and controls. Significantly higher RFI of FoxP3 expression in children with allergy than in healthy controls (median (25 percentile; 75 percentile): 11.4 (9.65; 13.53), 6.8 (5.35; 8.94), respectively, p=0.00004) was found. RFI value was significantly lower in the subgroup of patients with CA, AR and AC compared to the group of patients with concomitant AD and/or FA (median (25 percentile; 75 percentile): 9.9 (6.56; 11.47), 13.5 (11.26; 20.98), respectively, p=0.007). CD69 expression on CD4+CD25^{high}, was significantly higher in allergic patients (n=11) compared to healthy controls (n= 23) (median (25 percentile; 75 percentile): 6.8 (3.74; 9.68) vs. 3.1 (1.90; 4.34) respectively, p=0.013). Accordingly allergic patients had significantly higher expression of CD71 compared to non-allergic controls (median (25 percentile; 75 percentile): 4.2 (2.59; 8.20) vs. 2.8 (1.37; 3.76), p=0.021). The same analysis was conducted after elimination of activated T effector cells by excluding CD4+CD25^{high}CD127+CD71+ cells. The frequency of CD4+CD25^{high}CD127-CD71+ cells did not differed between allergic children n= 6: 3.5 (2.59; 5.87), and control group n=20: 3.83 (1.82; 5.00). We conclude that CD4+CD25^{high}FoxP3+CD127^{low}Tregs display substantial deficiencies in atopic patients as compared with healthy children, especially in multiorgan disease, compared to patients with single organ manifestations. Additionally, there is an association between Tregs and the sIgE serum concentration. Although Treg deficiency is not the only abnormality of immune regulation in atopy, better quantitative and qualitative characterization of Tregs in allergy is needed, because the decrease in the number and function of these cells may lead to down-regulation of T cells tolerance and exacerbate the disease.