Increased percentages of Th17 cells showed an association with poorly controlled bronchial asthma in the childhood

Bronchial asthma (BA) in childhood is the most common chronic disease estimated to affect up to 10% of all children. Moreover, the observed increase in the incidence of asthma relies mainly on the rise in childhood BA. It is well-established that BA is an immune-mediated complex and heterogeneous disease, characterised clinically by bronchial reactivity, intermittent but reversible obstruction, and chronic airway inflammation due to the infiltration with various immune cells (T lymphocytes, mast cells, basophils, IgE-producing plasmocytes) [1].

Intensively investigated for the last years was IL-17-driven inflammation in BA. After pathogen or allergen irritation, a subsequent differentiation of naive T lymphocytes into IL-17 producing cells was also observed. Th17 lymphocytes secrete various cytokines, such as IL-17A, IL-17F, and IL-22, which contribute to the well-establish broad range of cytokines (IL-4, IL-5, IL-6, IL-8, IL-12, IL-10, IL-13, IFN-γ) described to be involved in the BA pathogenesis. Th17 cells play a role in maintaining the respiratory inflammation by inducing mucosal and innate immune cells to secrete more inflammatory cytokines and chemokines that locally attract further mast cells, eosinophils, and basophils. Nevertheless, Th17 subpopulation of lymphocytes and their closely related IL-17A and IL-17F cytokines were also claimed guilty for mucin production, airway smooth muscle hyper reactivity and corticosteroid-resistant inflammation [1]. Although the intense scientific work on the role of Th17 in BA, studies involve pediatric patients are limited.

In our recent cross-sectional study (Velikova et al., Allergol Immunopathol, 2018), we aimed to assess the percentage of Th17 cells along with IL-17 levels in peripheral blood in 42 Bulgarian children with BA, and in control groups of pediatric patients with cystic fibrosis (CF) and healthy ones. We suggested that locally secreted IL-17 would be associated with elevated circulating Th17 cells, which can be detected in peripheral blood [2]. We recruited 20 children with BA, 12 with cystic fibrosis (CF) and ten healthy children without a history of allergies, aged 4-17 years. The percentages of Th17 cells were determined in peripheral blood by flow cytometry by the cell surface expression markers as follows: CD, CD4, CD161, CCR6, whereas the serum level of IL-17A was measured by ELISA.
We found that BA children had a significantly higher percentage of Th17 (12.40 ± 1.16%) in comparison with CF children (7.64 ± 0.87%, p = 0.0035) and healthy controls (7.25 ± 0.45%, p = 0.008). Furthermore, the percentage of Th17 cells was significantly increased in the peripheral blood of children with severe and poorly controlled BA (p < 0.001, post hoc, Bonferroni correction). Interestingly, patients with moderate BA had Th17 cells close to those in CF and healthy children. We found also that BA children with higher percentages of Th17 cells had a significantly higher number of attacks over the last 12 months (3.2 vs. 2.1, p = 0.028), higher percentage of nasal eosinophils, and worsen performance at lung function tests (FEV1 90.84 vs. 96.75, and a positive bronchodilator test in 5/11 vs. 8/9, p = 0.034). We did not find a relationship between the percentages of Th17 cells and the age of BA onset, the duration of the disease; and the administered therapy.

The levels of IL-17A were observed similar in all groups of children, and a correlation between the Th17 cells in peripheral blood and the concentration of IL-17 in serum was not found. This finding is not surprising since we investigated the peripheral blood, whereas the excessive attraction of neutrophils along with Th17 and IL-17A inflammation happens in the airways. Furthermore, all these factors were shown to be involved in the hyper production of mucin, the enhanced contractibility of the airway smooth muscle cells and the corticosteroid resistant airway inflammation in mouse models.

Similar results were obtained from Kerzel et al. (2012) who found higher percentages of Th17 lymphocytes in children with BA than in healthy subjects [3]. However, we also included a group of patients with CF as a control group and stratified the BA group in children with poor and better control of asthma. Thus, our results concerning the percentage of Th17 lymphocytes in the different groups of children with chronic obstructive lung disease are a theoretical contribution in the field of childhood BA for both Bulgarian pediatric science and worldwide.

Our results confirmed the significantly increased Th17 cells in peripheral blood of children with BA, especially in those with severe and poorly controlled BA, suggesting that in severe asthma, airway inflammation is driven simultaneously by Th2 and Th17 lymphocytes. Hence, targeting Th17/IL-17 could be of benefit for children with severe asthma. However, this should be considered with pronounced caution having in mind the heterogeneity of the disease and the physiological functions of Th17 cells in the human body. Therefore, it is a need for large randomised placebo-controlled clinical trials which to establish the benefit/risk profile of the targeted therapy.

REFERENCES

