Objectives: To evaluate the quantitative statuses of peripheral CD4+ T subpopulations in patients with gout and further investigate the effects of immunomodulatory combination therapies on those cells.

Methods: Total 247 patients who met the clinical criteria of gout from the American College of Rheumatology and 206 healthy controls (HCs) were enrolled in this retrospective cross-sectional study. Among those patients, 70 follow-up patients donated their peripheral blood after receiving immunomodulatory drugs (e.g., low-dose interleukin-2, rapamycin, metformin, retinoic acid, etc.). The absolute numbers of Th1, Th2, Th17 and Tregs in peripheral CD4+ T subsets were detected by flow cytometry combined with standard absolute counting beads.

Results: Compared with HCs, the absolute numbers of Th1 and Th17 were evidently increased in gout patients (P<0.001), while the level of Tregs was significantly decreased (P<0.05) (Figure 1). After immunomodulatory combination treatments, the cell ratio was greatly increased, especially the ratio of Tregs (P<0.001), while the level of Teffs was evidently decreased in gout patients (<0.001), while the level of Tregs was evidently increased in gout patients (<0.05) (Figure 2). After immunomodulatory combination treatments such as Th2/Tregs, restoring immune homeostasis (Figure 2).

Conclusion: This cross-sectional study clarified the abnormal statuses of CD4+ T subsets in gout patients, suggesting that CD4+ T subsets, especially Tregs, might be relevant and play a crucial role in the pathogenesis of gout, thus providing a potential therapeutic target for gout patients. Immunomodulatory combination therapies effectively increase the number of Tregs and may help for gout patients’ symptom remission.

References:

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AB0033
CHARACTERIZATION OF THE PERIPHERAL B CELL COMPARTMENT IN PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS
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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare form of systemic vasculitis, which is characterized by bronchial asthma, hypereosinophilia, and systemic vasculitis. B-lymphocytes play a key role in EGPA as producers of IgE and anti-neutrophil cytoplasmic antibodies (ANCAs). Indeed, the neutrophils that are targeted by these antibodies are widely described as the mechanism of endothelial damage in this disease. On the other side, the therapeutic response to rituximab in EGPA patients provides evidence for a role of B-cells in the pathogenesis of EGPA. Therefore characterizing B cell subpopulations may help in understanding the disease and the treatment.

Objectives: To characterize the peripheral B cell compartment in patients with EGPA and to analyze the in vivo potential of B lymphocytes to class-switch to IgE and to assess in vitro the differentiation potential of naïve B cells of EGPA patients into IgE-secreting plasmablasts.

Methods: Clinical characteristics of the patients, including organ involvement and treatment regimen were evaluated. Laboratory work-up included ANCA-status, eosinophils, IgE, IgG, IgA, IgM, and peripheral CD19+ B-cell count. For immunophenotyping isolated PBMCs were stained with monoclonal or polyclonal antibodies and B cells were classified into: naïve, marginal zone, class-switched memory B cells, unclassifiable memory B cells, transitional and plasmablasts. Furthermore, the expression of IgG- and subclasses IgG1-4, IgA, IgE B cells, BAFFR and TACI was quantified. For in vitro differentiation assays magnetically isolated B lymphocytes from EGPA patients and age-matched healthy controls were stimulated with CD40L, IL-21 and IL-4. Starting the culture with equal number of B cells, the absolute number of plasmablasts, and IgE class switched cells after 9 days was determined by counting the events in the CD27hiCD38hi gate or the IgGα/D-IgE+ gate by flow cytometry. IgE secretion in the supernatant was measured by ELISA.

Results: 34 patients with EGPA diagnosed according to ACR and CHC-criteria were included into the study. Ten of these patients were analyzed separately because they received rituximab therapy. Peripheral B cell numbers in EGPA patients were markedly diminished. B cell subpopulation phenotyping showed in average 57.9% naïve B cells, 12.5% marginal zone like B cells and 19.2% switched memory B cells. Plasmablasts constituted in average 1.15% of the peripheral B cell compartment, transitional B cells 2.0%. Interestingly, the expression of BAFF receptor and TACI in the memory B cell subset was significantly decreased in EGPA patients when compared with healthy donors. In vitro assays of isolated B cells from EGPA patients demonstrated an increased proportion of IgE-class-switched B cells after 9 days of culture under IL-4 stimulation compared with controls. However, no differences were observed in the phosphorylation of STAT5 and STAT6 after stimulation with IL-4 or IL-21.

Conclusion: In the EGPA-patients we observed markedly diminished B-cells despite of normal lymphocyte counts. B cells showed a reduced expression of BAFF-R and TACI. Class switch to IgE is enhanced in EGPA patients.

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AB0034
EARLY IMMUNIZATION AGAINST TREATMENT IS ASSOCIATED TO POOR CLINICAL RESPONSE AT 6 MONTHS AND LOW NUMBER OF TRANSITIONAL B CELLS AT BASELINE IN RHEUMATOID ARTHRITIS PATIENTS TREATED BY ADALUMAB
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Background: Circulating anti-drug antibodies (ADAs) are detectable progressively in 33% of adalimumab treated rheumatoid arthritis (RA) patients, often within the first 6 months of therapy1.2. Classically, circulating ADAs associate with their specific drugs to form immune complexes, increasing drug clearance, and by this mechanism reducing therapeutic effect. B cell involvement leading to circulating anti-drug antibodies is an established phenomenon2.3.

Objective: To analyze the impact of early interferon-alpha treatment on the clinical outcome and the ADA status of RA patients treated with adalimumab.

Methods: A total of 31 early interferon-alpha treated RA patients were compared with 50 non-treatment early interferon-alpha patients. Clinical characteristics were compared with Kruskal-Wallis test. ADA status at 6 months was compared with Fisher exact test. A multivariate regression analysis was conducted with the clinical outcome as dependent variable and ADA status at 6 months and age as independent variables.

Results: Early interferon-alpha treated RA patients showed a poorer clinical outcome compared with early interferon-alpha untreated patients (P < 0.05). The ADA status at 6 months was significantly associated to the clinical outcome (P < 0.05). A multivariate regression analysis confirmed this association (P < 0.05).

Conclusion: Early interferon-alpha treatment is associated to a poorer clinical outcome and to a higher ADA status at 6 months in early interferon-alpha treated RA patients treated with adalimumab.

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