ABERRANT PD-1 AND VISTA EXPRESSION ON CD4+ TH-CELLS IN GIANT CELL ARTERITIS

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Background: The immune system controls immune responses by balancing positive and negative immune checkpoint (IC) molecules in cell-cell interactions. These co-stimulatory and co-inhibitory molecules allow complete T-cell activation and T-cell effector functions giving rise to an optimal immune response while preventing autoimmunity (1). Failure of tolerance results in the initiation and propagation of pathogenic T-cell responses leading to the development of autoimmune diseases such as Giant Cell Arteritis (GCA). The latter is a complex illness of multiple pathogenic factors with important contributions of both innate and adaptive immunity in its initiation and perpetuation (2,3). Recently, a loss of inhibitory checkpoints on immune cells has been implicated in the immunopathology of GCA (4,5). The possible contribution of IC pathways to the dysregulation of Th-cells in GCA could aid in our understanding of GCA immunopathology.

Objectives: In this study, we aimed to investigate the expression of different IC molecules and their ligands by circulating monocytes, and functionally distinct populations of CD4+ T-cells in peripheral blood samples from GCA-patients in comparison to healthy controls (HCs).

Methods: In a cross-sectional study, fresh blood samples were obtained from 30 GCA-patients with/without immunosuppressive treatment (glucocorticoids) and 18 sex and age-matched HCs. The frequency of the expression of different IC including CD80/86, PD-L1, PDL2 and V-domain Ig suppressor of T-cell activation (VISTA) were determined on total monocytes and subsets (classical, intermediate and non-classical). In parallel, expression of the corresponding receptors CD28, Cytotoxic T-Lymphocyte-associated antigen-4 (CTLA-4), Programmed death-1 (PD-1), and VISTA were determined on total CD4+ and subsets of CD4-cells defined by CD45RA and CD25 expression of GCA-patients and HCs by flow cytometry.

Results: The frequencies of CD80/CD86+ and VISTA+ monocytes were decreased in GCA-patients compared to HCs. Proportions of circulating CD4+ T-cells in GCA-patients were not different when compared to HCs. The frequencies of CD25 and CTLA-4 expressing CD4+Th-cells did not differ between GCA-patients and HCs. In contrast, proportions of PD-1 and VISTA expressing Th-cells were significantly decreased in GCA patients. Memory T-cells showed decreased expression of IC molecules. Interestingly, naïve T-cell populations already demonstrated loss of PD-1 and VISTA.

Conclusion: In GCA, lower frequencies of CD80/CD86+ and VISTA+ circulating monocytes were found. Likewise, decreased proportions of PD-1+CD4+ and VISTA+CD4+ Th-cells were noted. Decrease of negative IC on the surface of immune cells could add to the persistent activation of CD4+ T-cells seen in GCA.

REFERENCES: