OXIDATIVE STRESS IMBALANCE MAY INFLUENCE IMMUNE SYSTEM FUNCTIONING IN MULTIPLE SCLEROSIS.

M. Gironi, M. Saresella, M. Vaghi, E. Mariani, C. Cursano, A. Angelini, R. Nemni, M. Clerici, M. Rovaris
Don Carlo Gnocchi Foundation (Milan, IT);
CAM, Polidiagnostic Center (Monza, IT)

Oxygen-derived free radicals can play a dual role in natural and acquired immunity and oxidative stress imbalance is widely reported in multiple sclerosis (MS). Oxidative stress may be detrimental in acquired immunity by activation of nuclear-factor-kappa B, a pro-inflammatory factor. In this study, we investigated whether a disequilibrium in oxidative stress markers is associated to peculiar immune signatures in MS.
In 30 untreated MS patients and 23 MS patients undergoing disease-modifying therapies (DMT) (matched for sex, age, disease duration and neurological disability) the intracellular expression of Transcription Factors (RORC, Tbet , GATA3) and IFNg,IL-4,TNFa,IL-9,IL-13,IL-17,IL-21,IL-22,IL-25, BDNF- producing CD4+ and CD8+ T cells and IL-6, IL12,IL-23, TGFb-producing CD14+cell percentage was analyzed by flow cytometry. Coenzyme-Q10, glutathione and malondialdehyde were determined by HPLC, reactive-oxygen-species (ROS) were photometrically quantified, anti-oxLDL were detected by ELISA, anti-oxidant-power was measured by the Cu++ reduction.
In untreated patients the following significant correlations were found: CD4IL22 with oxidized-glutathione (r=0.46) and malondialdeide (r=0.43), CD14IL6 with anti-oxLDL (r=-0.46) and CD4IL22 with anti-oxidant-power (r=-0.41). In patients treated with DMT, CD4IL22 significantly correlated with oxidized-glutathione (r=0.47), CD4IL4 with Coenzyme-Q10 (r=0.6), reduced glutathione with CD4IL25 cells (r=0.46) and CD8BDNF with anti-oxLDL(r=0.48).
In treatment-naive MS patients a decreased antioxidant cellular response was related to higher TH17 cell activation, while a marker of oxidative stress (oxidized-glutathione) positively correlated with the same immunophenotype. In patients treated with DMT, strong correlations were found between TH2 cells and beneficial antioxidant molecules (Coenzyme Q10, reduced glutathione). In addition, a suppressive response driven by CD8BDNF was related to antioxLDL, also endowed with a protective reparative role. These findings suggest that the relationship between oxidative stress and immune system functioning in MS might be, at least partially, modulated by DMT.