CD138+ PLASMA CELLS BUT NOT CD20+ B CELLS EXHIBIT CYTOTOXIC BEHAVIOR IN MS PATIENTS

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Backgroud: During relapsing-remitting MS (RRMS), CD8+ T lymphocytes infiltrate into the central nervous system (CNS) being found close to oligodendrocytes and neurons. Moreover, in severe/fatal MS relapses a massive infiltration of CD8+ T cells expressing granzyme B (GzmB) was described in CNS parenchyma, evidencing an aberrant cytotoxic behavior. At the same time, B cells and other subsets were demonstrated to share cytotoxic behavior in several diseases. **Objectives**: Since cytotoxicity is thought to be a central mechanism for neurodegeneration, we intend to investigate whether "cytotoxic" B cells occur in RRMS patients. **Methods:** We studied 104 RRMS patients [divided according treatment: Untreated, Glatiramer Acetate (GA), Interferon-β (IFN), Fingolimod (FTY) and Natalizumab (NTZ)] and 58 healthy donors. GzmB-derived CD19+ B cells was accessed in the peripheral blood from patients and healthy subjects using flow cytometry analyses (FACS). **Results:** Increased percentage of CD19+GzmB+ B cells was observed in FTY and NTZ subgroups when compared to GA, IFN and untreated RRMS patients. Moreover, using high-dimensional FACS (tSNE, UMAP), we observed that CD19+CD138+ plasma cells, but not CD19+CD20+ B cells, seem to represent a main subset of B cells involved in GzmB-expression. **Conclusions:** In addition to antigen presentation and cytokine production, ectopic cytotoxicity may represent a novel antibody-independent mechanism derived from B cells with possible implications for MS pathophysiology. Further investigations, in larger cohorts, may elucidate the clinical, and eventually therapeutic, relevance of "cytotoxic" B cells for MS.