MS treatment dilemmas: anti-T- or anti-B- cell regimens?

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Multiple Sclerosis (MS) is a chronic autoimmune demyelinating disorder of the central nervous system (CNS), mainly affecting young people. More than 13 disease modifying treatments are (DMTs) are currently available, aiming to control the disease activity, i.e., the inflammatory demyelinating attacks in the CNS parenchyma clinically expressed as relapses and the ongoing disability progression. The vast majority of DMTs target the activation of adaptive immunity, particularly the T-cells and concomitant T-cell – related immune reactions. However, there is increasing evidence that B-cells are also important players in the underlying immunopathology of the disease, as indicated by the presence of plasma cells, myelin-specific antibodies (Abs) and, to a lesser extent, B cells in both chronic MS plaques and acute MS lesions. In addition, the presence of immunoglobulins in MS CNS tissues, lymphoid-like tissues in MS CNS, B cells and plasma cells in MS cerebro spinal fluid (CSF), immunoglobulins in CSF and autoantibodies targeting myelin proteins in of MS patients highlight the B-cell involvement in MS immunopathology. In addition, it has been shown that Abs extracted from MS CNS tissue are often autoreactive with myelin Abs to non-protein CNS antigens in MS (though not specific for the disease) where as the presence of B cells characterizes the subtype II MS lesions which benefit from plasmapheresis. B cells can contribute to the pathogenesis of MS through cytokine production, antigen presentation and formation of autoantibodies. T- and B- cells do not function independently. B cells can activate autoreactive T cells; in return, T cells signal to B cells to enable maturation to plasma cells, which produce highly specific antibodies. These findings indicate the importance of targeting B-cells in order to control the disease activity. Interestingly enough, there is some evidence that even currently available DMTs have some effect on B-cells thus resulting in a shift in circulating B-cell immunophenotypes, thus increasing the relative frequency of immature and naive B cells, decreasing the proportion of memory B-cells, increased B-cell production of IL-10 with concurrent suppression of proinflammatory cytokine secretion. B cells from DMT-treated patients are generally less able to support a proinflammatory T-cell response. There is increasing recent evidence that DMTs targeting exclusively CD-20 on B-cells are able to control MS relapses and ongoing disability progression even in progressive forms of the disease. Among them, rituximab and ocrelizumab are typical examples of and-CD20 MAbs in MS. Evidently, despite the enrichment of our armamentarium to control MS, there is much concern in which cases should the anti- B- cell treatment be used and what the biomarkers indicating the predominant activity in an individual case might be.