The Characterisation of Ectopic Germinal Centres in MG

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Abstract

Myasthenia Gravis or MG is a rare autoimmune disease, in which autoantibodies that target receptors involved in neurotransmission, primarily the acetylcholine receptor (AchR), are generated in excess, resulting in severe muscle weakness. However, MG is particularly unique in that it is frequently associated with pathologies of the thymus, such as hyperplasia and ectopic germinal centre (eGC) formation, which are thought to be the source of the autoantibody production. This provides us with an exceptional opportunity to characterise the pathogenic alterations that drives the autoimmunity. Consequently, we have isolated and phenotypically evaluated different cellular subsets within the thymus, together with pair blood samples, of MG patients undergoing a thymectomy, using multi-colour flow cytometry. As previous literature describes, eGCs are most prevalent in the thymus of patients with early-onset MG (EOMG). Our FACS results corroborate this finding, as only patients diagnosed with EOMG contained T follicular helpers (Tfh) and regulators (Tfr), as well as GC B cells in their thymic tissue. However, we saw no difference in circulating Tfh and Tfr cells when compared to other subgroups of MG or sex- and age-matched controls. Nevertheless, we do find abnormalities in the proportion of several cellular constituents of the germinal centre within the thymus of MG patients. We are continuing to explore the mechanism of how this dysregulation contributes to persistence of the autoimmunity.