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B CELL RELATED PREDICTIVE BIOMARKERS OF TREATMENT RESPONSE IN MYASTHENIA GRAVIS

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Background and aims

Myasthenia Gravis (MG) is a B cell-mediated autoimmune disease characterized by muscle weakness and fatigability, mostly associated to antibodies against the acetylcholine receptor (AChR). MG patients are chronically treated by immunosuppressants and 10-15% are treatment refractory[1]. The purpose of our study is to identify changes in B-cell subsets that could predict treatment response in MG subgroups with different treatment-related status, with the aim of improving MG management, leading to personalized therapy.

Methods

Peripheral blood mononuclear cells (PBMCs) were isolated from 79 AChR-MG patients for the characterisation of transitional ($CD19^+CD20^+CD24^+CD38^+$), naïve ($CD19^+CD20^+IgD^+CD27^-$), double negative ($CD19^+CD20^+IgD^-CD27^-$), unswitched memory ($CD19^+CD20^+IgD^+IgM^+CD27^+$), switched memory ($CD19^+CD20^+IgD^-CD27^+IgG^+$) B-cells and plasmablasts ($CD19^+CD27^+CD38^+$) by multicolour flow cytometry.

Results

Thirty/79(38%) patients were women and mean age at onset was 48 years. At sampling, 15/79(19%) patients were immunotherapy-naïve, 38/79(48%) were immunotherapy-responders, 13/79 (16%) were refractory to standard immunotherapy and 25/79(36%) were in clinical stable remission (CSR). The frequency of total B-cells in the lymphocyte gate did not differ among the clinical subgroups. Naïve B-cells were lower (Fig.1A) in immunotherapy-responders compared to immunotherapy-naïve (p=0.005), refractory and patients in CSR (p=0.009). Transitional B-cells were increased in refractory MG compared to immunotherapy-naïve (p=0.01) and responders (p=0.029). Surprisingly, plasmablasts were lower in refractory patients than immunotherapy-naïve patients (Fig.1C) (p=0.018).

Discussion

The persistence of transitional B-cells, rather than antigen experienced B-cells, might predict unresponsiveness to immunotherapy in a subgroup of patients[2]. In these cases, B cell-directed therapies could restore the balance between regulatory and inflammatory B-cells in the pre-germinal compartment.

References

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