Organised B Cells and Plasma Cells in the Aorta of Giant Cell Arteritis Patients

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Background: Giant cell arteritis (GCA) is the most common type of systemic vasculitis. Currently, two forms of GCA are described: a cranial(C)-GCA and a systemic, large-vessel (L)-GCA. L-GCA frequently occurs without specific symptoms and late complications are aortic aneurysms or aortic rupture. Based on the analysis of temporal artery biopsies (TAB), GCA is postulated to start at the adventitial site and to be T cell-mediated. In the temporal artery infiltrates, T cells clearly outnumber B cells. Interestingly, we recently documented decreased numbers of B cells and elevated BAFF levels in newly diagnosed GCA patients. The predominance of organised B cells at the site of inflammation in LV-GCA suggests an involvement of B cell-mediated immune mechanisms in LV-GCA to be further explored.

Conclusions: In conclusion, aorta tissues from patients with histologically-proven LV-GCA showed massive B cell infiltrates, predominantly located in the adventitia, that were organised into ATLs. Moreover, these ATLs frequently contained plasma cell survival niches. The predominance of organised B cells and plasma cells at the site of inflammation in LV-GCA suggests an involvement of B cell-mediated immune mechanisms in LV-GCA to be further explored.

Disclosure of Interest: None declared


Non-Response to Rituximab Therapy in Reumatoid Arthritis Associates with Incomplete Disruption of the B-Cell Receptor Repertoire in the Peripheral Blood


Background: Rituximab (RTX) induces more than 98% depletion of the CD20+ B cells in blood after a single injection, yet 35% to 50% of RA treated patients show a poor response to the therapy. Despite the identification of many different biomarkers, mostly in the B cell compartment, adequate prediction of response to RTX treatment is still quite challenging.

Objectives: To test the hypothesis that non-response to rituximab can be predicted by analysing B-cell receptor (BCR) repertoire characteristics before and shortly after rituximab therapy.

Methods: Paired peripheral blood (PB) samples and synovial tissue (ST) samples were available from a total of 21 patients before therapy with RTX, and at 4 and 16/24 weeks after treatment. Next-generation sequencing was used to analyse the BCR repertoire, and assess the frequency of high expanded clones (HECs >0.5% of the sequenced reads) and load of somatic hypermutation (SHM). Clinical response was evaluated at 6 month following EULAR response criteria.

Results: In spite of the complete depletion of B cells (measured using CD19) with conventional flow cytometry, we detect a complete BCR repertoire at week 4 and 16/24 after RTX treatment. The post-treatment PB BCR repertoire is composed of fewer, but more expanded and more mutated clones compared to baseline (figure 1). Non-response associates with a higher number of HECs at week 4 (p<0.01) and with a higher overlap in the top-50 clones between the baseline and week 4 repertoire (p=0.03). In fact, in all non-responders some of the HECs detected at week 4 were already present at baseline. In these persisting clones the SHM load was higher than the median in the total repertoire. In the synovial tissue BCR repertoire the number of clones and HECs does not significantly change after RTX treatment. Like in PB, an increase in SHM load is observed after treatment but at the late time point (week 16). In ST the overlap within the top-50 clones with baseline is largely maintained at week 4, but then decreases at week 16. No baseline predictors of response to RTX treatment were identified.

Conclusions: Incomplete depletion of the baseline BCR clonal repertoire in peripheral blood within the first month of treatment predicts poor clinical response at 6 months, revealing the persistence of “rituximab-resistant” BCR clonal signatures associated with treatment failure. In all patients the PB BCR repertoire at 4 weeks after rituximab is dominated by few but highly expanded and highly mutated BCR clones, most likely CD20-negative plasmablasts, while less pronounced and delayed effects are observed in the ST BCR repertoire.

Disclosure of Interest: None declared