Objectives: We aimed to investigate the proportion and phenotype of peripheral blood ABCs in patients suffering from early drug naïve RA.

Methods: Newly presenting patients, naïve to immunomodulatory RA treatment, were recruited from the Newcastle Early Arthritis Clinic, and followed until diagnoses were confirmed. B-cell subsets in peripheral blood were detected and phenotyped using flow cytometry.

Results: Our work showed increased proportions of ABCs in seropositive RA compared to other inflammatory arthritis controls, highlighting a potential link between autoantibody production and ABCs. Moreover, patients with high disease activity had higher proportions of ABCs in peripheral blood. Interestingly, the FcRL4+, the proliferating Ki67+, and the T-bet expressing B cells were enriched in the ABC population compared to the other B cell subsets. Furthermore, ABCs expressed high levels of MHC class II and co-stimulatory molecules, as well as the activation marker, CD69.

Conclusions: This study supports a possible pathogenic role of ABCs in RA, potentially via autoantibody and T cell stimulatory activity, but further characterisation of this subset and functional studies are needed.

Disclosure of Interest: None declared


THU0034
SALMONELLA TYPHI VI IGG AS A MARKER OF IMMUNOSUPPRESSION IN RHEUMATIC DISEASE

L. Williams1, G. Candelas2, C. Tarro1, J. Ochoa-Gruñón3, P. Macamón3, C. Morado3, K. H. Llanza4, C. Martínez-Prada5, A. Rodríguez de la Peña6, B. Fernández7,2, J. S. Harding8, S. Sanchez-Ramón1, A. Parker1,1

The Binding Site Group Ltd, Birmingham, UK
2Department of Rheumatology, Hospital Clínic San Carlos, Madrid, Spain

Background: Measurement of vaccine response may be used as a diagnostic tool to aid determination of antibody deficiency. The IgG response to pneumococcal polysaccharide vaccination (PPV) is currently used to assess T cell independent responses, however additional polysaccharide vaccines are under evaluation. In patients with rheumatoid diseases (RD) treatment regimens can result in immunosuppression and subsequently secondary immune deficiency (SID).

Objectives: To measure the IgG response to Typhi Vi vaccination (TV) in RD patients presenting with antibody deficiency. To correlate immunosuppression with TV responses, as well as TV responses to clinical presentations, B cells and total IgG. Further, we interpret the responses in combination with the responses to PPV.

Methods: 35 RD patients were referred for immunological evaluation at Hospital Clínic San Carlos, Madrid, Spain. The responses to TV and PPV were measured using commercial human anti-Salmonella Typhi Vi IgG and pneumococcal capsular polysaccharide (PPV) IgG ELISAs kits. A TV responder was defined as achieving >32 IU/mL (lower limit of the normal range), a PPV IgG responder (>90 mg/L). B cells were measured by flow cytometry (responder >6.6%) and total IgG by nephelometric assay (responder >600 mg/dL). For all measurements, a (−) indicates a non-responder and (+) indicates a responder.

Results: A greater proportion of TV- patients previously received non-biologic treatment (79% vs 43%), specifically steroid treatments (68% vs 28%) and biologic treatments (particularly CD20 and TNF alpha targets; 46% vs 14%). At presentation, TV non-responsiveness was associated with a higher frequency of upper respiratory tract infections (75% vs 57%), serious bacterial infections (21% vs 16%) and patients requiring surgical intervention (50% vs 71%). Stratification of the RD patients using the response to TV and PPV identified four groups of activity: TV−/PCP−, TV−/PCP+, TV+/PCP− and TV+/PCP+.

In the presence of a normal response to PPV, the failure to respond to TV correlated with a higher frequency of previous non-biologic treatment (84% vs 43%), biological treatment (47% vs 14%), steroids treatment (68% vs 28%) and were currently undergoing treatment (84% vs 29%, p<0.01) compared those who responded to TV (TV+/PCP+). At presentation TV−/PCP− patients had a higher incidence of upper respiratory tract infections (74% vs 57%), serious bacterial infections (16% vs 14%) and antibiotic usage (95% vs 71%). Non-responders to both vaccinations (TV−/PCP−) had a higher incidence of serious bacterial infections (25% vs 16%) and pneumonia (50% vs 32%) when compared to the TV−/PCP+ group. When correlated with B cell number, 56% of B cells had a concentration of TV antibodies <32 IU/mL.

Conclusions: The response to TV correlated with underlying disease treatment and immunological presentation. Assessing the response to two polysaccharide vaccinations, TV and PPV, may provide a greater understanding of the T cell independent pathway and provide more clinical information for the clinician.

Disclosure of Interest: None declared


THU0035
A CD8 ALPHA-NEGATIVE SUBSET OF CD4+SLAMF7+, CYTOTOXIC T CELLS IS EXPANDED IN PATIENTS WITH IG4-RELATED DISEASE AND DECREASES FOLLOWING GLUCOCORTICOID TREATMENT

F. De la Torre1, E. Bozzailla Cassione1, C. Sciorati2, M. Lanzillotta1, E. Bozzolo1, L. Rovati1, H. Mattoo2, C. Perugino3, I. Stone4, L. Dagnn4, S. Pillia5, A. Mantredi6
1Unit of Immunology, Rheumatology, Allergy and Rare Diseases, IRCCS-Ospedale San Raffaele, Milan, Italy
2Ragon Institute of MGH, MIT, Harvard
3Unit of Rheumatology, Massachusetts General Hospital, Boston
4Ragon Institute of MGH, MIT, Harvard, Cambridge, USA
5Autoimmunity and Vascular Inflammation, IRCCS-Ospedale San Raffaele, Milan, Italy

Background: IgG4-Related Disease (IgG4-RD) is a fibro-inflammatory disorder characterised by tumefactive lesions, frequent elevation of serum IgG4 levels, and tissue fibrosis. Glucocorticoids represent the treatment of choice to induce IgG4-RD remission but their effect on the cells orchestrating the disease remains unknown.1 We recently described an unconventional population of clonally expanded CD4+SLAMF7+ cytotoxic T effector memory (TEM) cells (CD4+CTLs) and causally linked it to IgG4-RD in view of their capacity to secrete pro-fibrotic molecules and to infiltrate affected organs.2,3

Objectives: In order to better clarify the mechanisms of action of glucocorticoids in IgG4-RD and the pathogenic relevance of CD4+ CTLs, we herein aim to describe the effects of corticosteroid treatment on CD4+ CTLs.

Methods: CD8+ lytic, granzyme A, perforin, and SLAMF7 expression within the effector/memory compartment of CD45RO (TEM and CD45RA (TEMRA) CD4+ T cells was quantified by flow cytometry in 18 active IgG4-RD patients at baseline and after 6 months of glucocorticoid treatment. Eighteen healthy subjects were studied as controls. Next-generation sequencing of the T-cell receptor β and γ chain gene was performed on circulating CD4+ CTLs in patients with IgG4-RD before and after treatment, and in affected tissues.

Results: Circulating CD4+ TEM and TEMRA cells were not expended in IgG4-RD patients compared to healthy controls. CD4+SLAMF7+ TEM cells (but not TEMRA cells) were significantly increased among IgG4-RD patients. Within CD4+SLAMF7+ TEM cells, CD8+/ but not CD8-bx/TEMRA cells were elevated in IgG4-RD patients. The same dominant clones of CD8+/CD4+SLAMF7+ TEM cells found in the peripheral blood were also identified in affected tissue. Both CD8+/CD4+TEMRA and CD4+SLAMF7+ TEM cells expressed cytolytic molecules. Clonally expanded CD8+ but not CD8+CD4+SLAMF7+ TEM cells decreased following glucocorticoid-induced remission.

Conclusions: A subset of CD8+CD4+SLAMF7+ cytotoxic TEM cells is oligoclonally expanded in patients with active IgG4-RD. This population contracts following glucocorticoid-induced remission. Further characterisation of this cell population may provide prognostic information and targets for therapeutic intervention.

REFERENCES:

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THU0036
ABATACEPT INCREASES REGULATORY B CELL EFFECT ON T CELL PROLIFERATION THROUGH THE PRODUCTION OF IL-10 AND TGF-BETA IN VITRO AND IN RHEUMATOID ARTHRITIS PATIENTS

G. Carvajal-Alegria1, P. Gazeau1, A. Saraux1, V. Devauchelle-Pensec1, D. Cornec1, J.-O. Pers1, P. Pochard2
1Rheumatology, CHRU Cavale Blanche
2UMR 1227 LBAI, CHRU Morvan, Brest, France

Background: Abatacept is a CD152 agonist known to inhibit T cell proliferation but recent data suggest that it could act directly on B cells.1,2

Objectives: To demonstrate the effect of Abatacept (versus IgG control) on regulatory functions of B cells on T cell proliferation in an established in vitro co-culture model. To evaluate its role, in vivo, by measuring the regulatory functions of B cells from rheumatoid arthritis patients before and after the Abatacept treatment.

Disclosure of Interest: None declared


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Methods: Peripheral and tonsilar T cell and B cell from healthy controls were purified. The biotinylation of Abatacept was used to study its binding on T and B cells by flow cytometry and confocal microscopy. A well-established co-culture model between CpG-stimulated B cells and anti-CD3/anti-CD28 stimulated T cells was set up in which Abatacept or an IgG control was added to evaluate any change in B cell regulatory functions. Activation markers (e.g. CD25, CD69, CD40, CD152) and regulation markers (e.g. Foxp3, TGF-β) were assessed by flow cytometry. Similar analysis were also performed on rheumatoid arthritis patients before and three months after Abatacept therapy. All patients gave their informed consent.

Results: Abatacept increases the inhibition of T cell proliferation by B cells compared to IgG control in the co-culture model (p<0.03). Interestingly, alone, Abatacept does not modify T cell proliferation. This can be explained by the increase in IL-10 and TGF-β producing B cells and the CD152 expression. Abatacept is able to bind B cells at day 0 of co-culture and T cells at day 4.5 of co-culture. Abatacept has a direct effect, also, on B cells by increasing the CD25 (p<0.03) and CD152 expression (p<0.02) reflecting a higher activation level. Nevertheless, Abatacept had no direct effect on B cell proliferation. In RA patients, the treatment with Abatacept resulted in an increased regulation of T cell proliferation and this effect is related to a higher percentage of IL-10 secreting B cells 3 months after the therapy (p<0.03).

Conclusions: In our in vitro and in vivo models, Abatacept has a direct effect on B cells leading to an increase capability of regulation of T cell proliferation which directly linked to higher production of IL-10 and TGF-β.

REFERENCES:

Disclosure of Interest: None declared

THU0038 INCREASE OF CIRCULATING MEMORY B CELLS AFTER GLUCOCORTICOID-INDUCED REMISSION IDENTIFIES PATIENTS AT RISK OF IGG4-RELATED DISEASE RELAPSE
M. Lanzillotta1, E. Della Torre2, R. Milanò3, E. Bozzolo1, E. Bozzalla Cassione1, L. Roveri1, M. Falconi1, F. Ciceri1, L. Dagni4. 1Internal Medicine, Allergy And Clinical Immunology; 2Unit of Hematology and Bone Marrow Transplantation; 3Unit of Pancreatic Surgery – Pancreas Translational and Clinical Research Center; 4Unit of Allergy, Clinical Immunology and Rare Disease – UniRAN, San Raffaele Scientific Institute, Milan, Italy

Background: IgG4-related disease (IgG4-RD) is relapsing-remitting systemic fibro-inflammatory condition characterised by elevated serum IgG4 concentration and by tumor-like lesions. 1 Glucocorticoids represent the treatment of choice to induce IgG4-RD remission but relapses occur in almost 50% of patients at two years. 2 Several evidences suggest that B cells are central to the pathogenesis of IgG4-RD, the most significant being (i) the clinical improvement induced by B cell depletion with rituximab, and (ii) the oligoclonal expansion of circulating plasma blasts in the vast majority of patients. 1,3

Objectives: To describe alterations of B lymphocyte subpopulations that might predict IgG4-RD relapse in patients treated with a first course of glucocorticoids according to international guidelines.

Methods: Thirty patients with IgG4-RD were treated with glucocorticoids according to international consensus guidelines. Flow cytometry analysis of circulating CD19+ and CD20+ cells, naïve B cells, memory B cells, plasmablasts, and plasma cells was performed at baseline and every 6 months after the initiation of corticosteroid treatment.

Results: Patients with active untreated IgG4-RD showed reduced CD19+ B cells, CD20+ B cells, and naïve B cells compared to healthy controls (p<0.05), but expanded plasmablasts and plasma cells (p<0.01). Glucocorticoids treatment led to disease response in all patients. Clinical improvement was accompanied by a significant reduction of naïve B cells, circulating plasmablasts, and plasma cells, and by a significant increase of memory B cells compared to baseline (p<0.01). Increase of circulating memory B cells was observed only in patients experiencing disease relapse and not in patients who maintained remission at two years of follow-up (HR:14.40, 95% CI 2.96–70.1, p<0.01, figure 1 A–B). Relapse rates at 12 and 24 months were 25% and 100% with memory B cell increase at 6 months (figure 1C), respectively. No B cell subpopulations were found to predict IgG4-RD relapse at disease onset.

Conclusions: The efficacy of glucocorticoids in IgG4-RD is associated with selective effects on different B-cell subpopulations. IgG4-RD relapse may be predicted by the increase of memory B cells after glucocorticoid-induced remission

REFERENCES: