OP0049

ABERRANT VISTA EXPRESSION ON CD45RA+CD25DIM TH-CELLS IN GIANT CELL ARTERITIS

R. Hid Cadena¹, R.D. Reitsema², W.H. Abdulahad^{1,2}, M.G. Huijtema², A.M. Boots², P. Heeringa¹, E. Brouwer². ¹Pathology and Medical Biology; ²Rheumatology and Clinical Immunology, University Medical Center Groningen, Groningen, Netherlands

Background: A broad naïve Th-cell repertoire is needed to face novel antigenic challenges and mounting an optimal immune response.^{1,2} The replenishment of naïve T-cells is severely restricted by thymic involution with ageing.³ In the past, our group provided new insight into the homeostasis of human Th-cells, identifying CD45RA⁺CD25^{dim}Th-cells as a subset of post-thymically expanded naïve Th-cells in healthy aged individuals.⁴ Immune homeostasis of naïve Th-cells is especially important to understand defective immune responses in age-related immune disorders such as Giant Cell Arteritis (GCA). Recently, a loss of immunoinhibitory checkpoints has been implicated in GCA.^{5,6} The possible contribution of immune checkpoint pathways to the dysregulation of Th-cells, especially in CD45RA⁺CD25^{dim}Th-cells in GCA has not yet been studied.

Objectives: In this study, we aimed to investigate the expression of different immune checkpoint molecules on circulating CD45RA⁺CD25^{dim}Th-cells of GCA-patients and compare it with matched healthy controls (HCs).

Methods: In a cross-sectional study, fresh blood samples were obtained from 33 GCA-patients with/without immunosuppressive treatment (glucocorticoids) and 12 sex/age-matched HCs. The frequency of the expression of different immune checkpoints including CD28, Cytotoxic T-Lymphocyte-associated antigen-4 (CTLA-4), Programmed death-1 (PD-1), and V-domain Ig suppressor of T cell activation (VISTA) were determined on CD45RA⁺CD25^{dim}Th-cells of GCA-patients and HCs by flow cytometry.

Results: Proportion of circulating CD45RA⁺CD25^{dim}Th-cells in GCA-patients was not different when compared to HCs, whereas significant increase in these cells was observed only in treated GCA-patients when compared to HCs. The proportion of CD28, CTLA-4 and PD-1 expression on CD45RA⁺CD25^{dim}Th-cells did not differ between GCA-patients and HCs. Interestingly, proportion of VISTA expression on these cells was significantly decreased in GCA-patients. Furthermore, decreased frequency of VISTA expression was seen in both untreated and treated patients.

Conclusions: In GCA-patients (untreated and treated), lower frequencies of VISTA⁺CD45RA⁺CD25^{dim}Th-cells were noted. Decreased VISTA expression in GCA-patients could play a role in the regulation of Th-cell activation/inhibition. The functional consequences of immune checkpoint modulation within particular subsets requires further investigation.

REFERENCES:

- [1] Nikolich-Zugich J, Slikka MK, Messaoudi I. The many important facets of T-cell repertoire diversity. *Nat. Rev. Immunol* 2004;4:123–132.
- [2] Goronzy JJ, Lee WW, Weyand CM. Aging and T-cell diversity. *Experimental Gerontology* 2007;42:400–406.
- [3] den Braber I, et al. Maintenance of peripheral naïve t cells is sustained by thymus output in mice but not humans. *Immunity* 2012;36:288–297.
- [4] van der Geest KSM, et al. Low-affinity TCR engagement drives IL-2-dependent post-thymic maintenance of naïve CD4⁺ T cells in aged humans. *Aging Cell* 2015;14:744–753.
- [5] Zhang H, et al. Immunoinhibitory checkpoint deficiency in medium and large vessel vasculitis. *Proc. Natl. Acad. Sci* 2017;114(6):E970–E979. doi:10.1073/pnas.1616848114
- [6] Onuora S. Vasculitis syndromes: Loss of immunoinhibitory checkpoint implicated in GCA. *Nat. Rev. Rheumatol* 2017;13:129–129.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2511

OP0050

GENE POLYMORPHISMS OF THE GLUCOCORTICOID RECEPTOR AND 11B-HYDROXYSTEROID DEHYDROGENASE TYPE 1 AFFECT RELEVANT CLINICAL OUTCOMES IN ANCA ASSOCIATED VASCULITIS

A.C. Hessels¹, J. Tuin¹, J.S.F. Sanders¹, M.G. Huijtema², E.F.C. van Rossum³, F.J. W. Koper³, A.P. van Beek⁴, C.A. Stegeman¹, A. Rutgers². ¹Internal Medicine – Nephrology; ²Rheumatology, University Medical Center Groningen, Groningen; ³Internal Medicine – Endocrinology, Erasmus Medical Center, Rotterdam; ⁴Internal Medicine – Endocrinology, University Medical Center Groningen, Groningen, Netherlands

Background: High doses of exogenous glucocorticoids (e.g., prednisolone) are a standard part of treatment for ANCA-associated vasculitis.¹ Efficacy and toxicity of glucocorticoid treatment differ widely between individuals.² We hypothesised

that this can be partly explained by genetic polymorphisms of the glucocorticoid receptor (GR) and 11 β -hydroxysteroid dehydrogenase type 1 (HSD11B1) that influence glucocorticoid sensitivity.

Objectives: To investigate whether five haplotypes of the Glucocorticoid Receptor gene (NR3C1) and a single nucleotide polymorphism of 11 β -hydroxysteroid dehydrogenase type 1 (HSD11B1) are associated with treatment efficacy and toxicity in ANCA associated vasculitis.

Methods: A total of 241 ANCA associated vasculitis patients were genotyped for five polymorphisms of the glucocorticoid receptor gene and one polymorphism of the HSD11B1 gene. Glucocorticoid receptor gene haplotypes were predicted based on genotyping results. Relapse free survival, mortality, renal survival, metabolic adverse events and infections were compared between carriers and non-carriers of glucocorticoid receptor haplotypes and the HSD11B1 genotype.

Results: Carriers of the ER22/23EK haplotype of the glucocorticoid receptor had a significantly higher risk of 10 year mortality (Hazard Ratio (HR) 3.0, 95% confidence interval, CI: 1.2 to 7.3), more frequently required plasmapheresis treatment (p=0.04) and had a higher risk of developing end-stage renal disease (HR 7.4, 95% CI: 1.9 to 28.7). Carriers of a minor variant of HSD11B1 more frequently experienced relapse (HR 2.5, 95% CI: 1.5 to 4.1), except if they also carried the BclI haplotype of the glucocorticoid receptor. Homozygous carriers of the BclI haplotype had a higher risk of developing hypertension (HR 2.7, 95% CI: 1.2 to 5.7) and dyslipidemia (HR 4.1, 95% CI: 1.8 to 9.6). Occurrence of infections neither differed between GR haplotypes, nor between HSD11B1 genotypes.

Conclusions: The ER22/23EK and BclI haplotype of the glucocorticoid receptor and a polymorphism of the gene for HSD11B1 are associated with clinically relevant inflammatory and metabolic outcomes in ANCA associated vasculitis.

REFERENCES:

- [1] Yates M, Watts RA, Bajema IM, Cid MC, Crestani B, Hauser T, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. *Ann Rheum Dis* 2016 Sep;75(9):1583–1594.
- [2] Quax RA, Manenschijs L, Koper JW, Hazes JM, Lamberts SW, van Rossum EF, et al. Glucocorticoid sensitivity in health and disease. *Nat Rev Endocrinol* 2013 Nov;9(11):670–686.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.1047

OP0051

EVOLUTION OF THE VASCULAR INVOLVEMENT OBJECTIFIED BY PET/TAC IN PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB

D. Prieto-Peña¹, J. Loricera¹, J. Martín-Varillas¹, M. Calderón-Goercke¹, J. Návárez², E. Aurecochea³, I. Villa³, S. Castañeda⁴, C. Gómez-Arango⁵, A. Mera⁶, E. Pérez-Pampín⁶, V. Aldasoro⁵, N. Álvarez-Rivas⁷, N. Fernández-Llano⁸, M. Álvarez-Buero⁹, L. Marena-Rojas¹⁰, F. Sivera¹¹, E. Galindez-Agirregoikoa¹², R. Solans-Laqué¹³, S. Romero-Yuste¹⁴, I. Martínez-Rodríguez¹, I. Banzo¹, V. Calvo-Río¹, N. Palmou-Fontana¹, B. Atienza-Mateo¹, J. Hernández¹, M. González-Gay¹, R. Blanco¹. ¹Departments of Rheumatology, Nuclear Medicine, Internal Medicine and Pathology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Universidad de Cantabria, Santander; ²Bellvitge, Barcelona; ³Sierrallana, Torrelavega; ⁴La Princesa, Madrid; ⁵Alto Deba, Mondagrón; ⁶CHU, Santiago de Compostela; ⁷Lucas Augusti, Lugo; ⁸Armau de Vilanova, Lérida; ⁹Río Carrión, Palencia; ¹⁰La Mancha Centro, Alcázar de San Juan; ¹¹Hospital de Elda, Elda; ¹²Hospital de Basurto, Bilbao; ¹³Valle-Hebrón, Barcelona; ¹⁴CHU, Pontevedra, Spain

Background: Giant cell arteritis (GCA) is a large-vessel vasculitis which can involve the aorta and/or its major branches. Tocilizumab (TCZ) seems to be effective in giant cell arteritis (GCA).^{1–4}

Objectives: Our aim was to assess if the clinical and analytical improvement yielded in patients with GCA treated with TCZ is accompanied by a reduction of the vascular inflammation evaluated by PET/CT.

Methods: Study of 36 patients who had a baseline and follow-up PET/CT from a multicenter series of 134 patients with GCA in treatment with TCZ. The evolution of the vascular involvement objectified by PET/CT was assessed. In addition clinical efficacy, analytical improvement (acute phase reactants) and the reduction of corticosteroid dose was studied.

Results: The 36 patients (28 women and 8 men) had an mean age of 69.83±8.66 years. After TCZ onset, a rapid and maintained clinical improvement was observed (table 1). In addition, during the first twenty-four months of follow-up, C-reactive protein decreased from 2.4 [0.9–6.8] to 0.1 [0.0–0.5] mg/dL and the erythrocyte sedimentation rate from 41.5 [16.7–58.5] to 4 [2–12.5] mm/1 st hour. On the other hand, the levels of haemoglobin experienced an increase from 12.3 [11.3–13.0] to 13.3 [13.0–13.9] g/dL. The median dose of prednisone decreased from 12.5 [9.4–26.2] to 0.0 [0.0–0.0] mg/day. However, the decrease in F18-fluorodeoxyglucose uptake in the PET/CT study was not as evident.