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-Llanio⁸, M. Álvarez-Buergo⁹, L. Marena-Rojas¹⁰, F. Sivera¹¹, E. Galíndez-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.

Abstract OP0051 – Table 1

	Baseline	Month 6	Month 12	Month 18	Month 24
Clinical improvement n, (%)					
Complete		28/35 (80)	24/27 (88.9)	21/22 (95.4)	17/18 (94.4)
Partial		5/35 (14.3)	3/27 (11.1)	1/22 (4.5)	1/18 (5.5)
No improvement		2/35 (5.7)	0 (0)	0 (0)	0 (0)
Laboratory markers, median [IQR] #					
ESR	41.5 [16.7-58.5] (36)	4 [2-8] (35) *	4.5 [2-12] (28) *	5 [2.5-11] (23) *	4 [2-12.5] (19) *
CRP	2.4 [0.9-6.6] (36)	0.1 [0.0-0.7] (33) *	0.3 [0.1-0.6] (27) *	0.1 [0.1-0.5] (23) *	0.1 [0.0-0.5] (18) *
Dose of corticosteroids (mg/day), median [IQR] #	12.5 [8.4-26.2] (36)	5.0 [1.2-5.0] (33) *	0.0 [0.0-4.2] (28) *	0.0 [0.0-2.5] (21) *	0.0 [0.0-0.0] (19) *
Improvement in PET/CT					
Complete		0/8 (0)	3/13 (23)	3/11 (27.3)	1/4 (25)
Partial		6/8 (75)	6/13 (46.1)	7/11 (63.6)	2/4 (50)
No improvement		2/8 (25)	4/13 (30.8)	1/11 (9.1)	1/4 (25)

*p<0.0001 (Wilcoxon test)

Conclusions: Although TCZ seems to be an important therapeutic agent in the treatment of GCA, achieving a rapid and sustained clinical and analytical improvement, the decrease in vessel inflammation assessed by F18-fluorodeoxyglucose uptake seems to take a slower course.

REFERENCES:

- [1] Loricera J, et al. Tocilizumab in giant cell arteritis: Multicenter open-label study of 22 patients. *Semin Arthritis Rheum* 2015;44:717–723.
- [2] Loricera J, et al. Tocilizumab in refractory aortitis: Study on 16 patients and literature review. *Clin Exp Rheumatol* 2014;32(3 Suppl 82):S79–89.
- [3] Loricera J, et al. Use of positron emission tomography (PET) for the diagnosis of large-vessel vasculitis. *Rev Esp Med Nucl Imagen Mol* 2015;34:372–377.
- [4] Loricera J, Blanco R, Hernández JL, et al. Tocilizumab in patients with Takayasu arteritis: A retrospective study and literature review. *Clin Exp Rheumatol* 2016;34(3 Suppl 97):S44–53.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4083

OP0052 MICROPARTICLES AS POTENTIAL BIOMARKERS OF DISEASE ACTIVITY IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY – ASSOCIATED VASCULITIS

A. Antovic¹, M. Kostic², F. Mobarrez¹, A. Nordin¹, J. Vojinovic², A. Bruchfeld³, I. Gunnarsson¹. ¹Department of Medicine, Rheumatology Unit, Karolinska Institutet, Stockholm, Sweden; ²Department of Pediatrics, Medical Faculty, University of Niš, Nis, Serbia; ³Department of Renal Medicine, Karolinska Institutet, Stockholm, Sweden

Background: Microparticles (MPs) are submicron particles, which are released from plasma membrane upon cell activation and during the early phase of apoptosis. Increased levels of circulating MPs, mainly of endothelial cell origin, but also platelet derived, have been shown to correlate with autoinflammatory disease activity, such as anti-neutrophil cytoplasm antibody (ANCA) – associated vasculitis (AAV).

Objectives: The aim was to evaluate levels of activity markers expressed on MPs from patients with AAV, during active disease and remission, compared to healthy control subjects.

Methods: Our study included 46 AAV patients and 23 healthy age and gender matched control subjects. We analysed the concentration of MPs in plasma by flow cytometry. MPs were phenotyped by expression: CD142 (tissue factor-TF), anti-H3cit (citrullinated Histone 3 directed against neutrophil extracellular traps – NETs), anti-pentraxin3 (pentraxin3), HMGB1 (high mobility group box 1 protein-HMGB1), anti-TWEAK (tumour necrosis factor-like weak inducer of apoptosis-TWEAK), anti-plasminogen (plasminogen), anti-C3a (C3a) and anti-C5a (C5a). The assessment of vasculitis disease activity was performed using the Birmingham Vasculitis Activity Score (BVAS), where active disease was defined as BVAS ≥ 1 and inactive (remission) as BVAS=0.

Results: Half of the patients group² had active vasculitis (13 male/10 female, mean age 61±14 years) and 23 had inactive disease (12 male/11 female, mean age 64±13 years). Concentration of MPs expressing TF, H3cit, pentraxin-3 and HMGB1 in active patients were significantly higher than in those in remission and healthy controls (p<0.01, p<0.0001, respectively). MPs expressing C5a and C3a were significantly higher in both active and inactive patients compared to controls (p<0.001). Additionally, levels of MPs expressing C5a and C3a strongly correlated with BVAS in patients with active disease (r=0.78, p<0.0001; r=0.5, p<0.01, respectively), while there was no significant correlation between other explored markers and BVAS.

Conclusions: Our results support recently postulated role of the complement system in AAV pathogenesis and disease activity. Evaluated proteins expressed

on MPs, especially C5a and C3a, could be used as potential biomarkers which might reflect inflammation and disease activity in AAV patients. Further investigations are necessary to confirm our preliminary results and to validate the most promising biomarker in AAV.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5465

OP0053 INFLAMMATORY DISORDERS ASSOCIATED WITH TRISOMY 8 MYELODYSPLASTIC SYNDROMES : FRENCH RETROSPECTIVE CASE CONTROL STUDY

N. Wesner¹, L. Drevon¹, A. Guedon², J.B. Fraison³, S. Trad⁴, J.E. Kahn⁵, A. Aouba⁶, J. Gillard⁷, M. Ponsioye⁸, T. Hanslik⁹, C. Gourguechon⁹, E. Liozon¹⁰, K. Laribi¹¹, J. Rossignol¹², O. Hermine¹², L. Ades¹³, F. Carrat², P. Fenaux¹³, A. Mekinian¹, O. Fain¹. ¹Internal Medicine, Inflammation-Immunopathology-Biotherapy Department (DHU i2B); ²Hôpital Saint Antoine; ³Hôpital Cochin, Paris; ⁴Hôpital Ambroise Paré, Boulogne Billancourt; ⁵Hôpital Foch, Paris; ⁶CHU, Caen; ⁷CH, Lons le Saunier; ⁸Hôpital Ambroise Paré, Boulogne Billancourt; ⁹CHU, Amiens; ¹⁰CHU, Limoges; ¹¹CH, Le Mans; ¹²Hôpital Necker Enfants Malades; ¹³Hôpital St Louis, Paris, France

Objectives: We report myelodysplastic syndrome (MDS)-associated systemic inflammatory and autoimmune diseases (IADs) with cytogenetic trisomy 8, and describe their outcome, treatments efficacy and impact on MDS survival in a French multicenter retrospective study.

Methods: In this study, 21 patients with trisomy 8-MDS and IADs were analysed and compared to 103 MDS patients with trisomy 8 without IADs.

Results: The median age was 67 [59 – 80] years and the male/female ratio 0.9. The IADs were Behçet's or Behçet's-like disease in 11 (52%) cases, inflammatory arthritis in 4 (19%) cases, Sjögren's syndrome, autoimmune hemolytic anaemia, aseptic abscesses, polyarteritis nodosa, Sweet's syndrome and unclassified vasculitis in one case each. Trisomy 8 karyotype was isolated in 8 cases (38%) and associated with other abnormalities in remaining cases. Seventeen (81%) IADs patients were treated (88% with steroids) with complete and partial response in 35% and 47%, respectively. A second-line therapy was required for steroid dependence or relapse in 38% of cases. The effect of MDS treatment on IADs could be assessed in 7 patients treated with Azacytidine : 5/13 (38%) achieved remission and 2/13 (15%) partial response of IADs. Compared with 103 trisomy 8-MDS/CMML patients without IADs, IADs patients were more often non-Caucasian (p=0.004), MDS subtype tended to be more frequently CRDM (p=0.09) and had more often a poor karyotype (p<0.001). No survival difference was seen between patients with trisomy 8-MDS-associated IADs and without IADs.

Conclusions: The spectrum of IADs associated to trisomy 8-MDS is dominated by Behçet's disease, but may also be other various immune disorders. Steroid therapy is often effective, but sparing therapies are mostly necessary.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3975

WEDNESDAY, 13 JUNE 2018

Envisioning new horizons for people with osteoarthritis

OP0054 PAIN IN HAND OSTEOARTHRITIS AND THE ASSOCIATIONS WITH RADIOGRAPHIC OSTEOARTHRITIS SEVERITY AND PSYCHOLOGICAL FACTORS

E. Mulrooney¹, K. Magnusson², H.B. Hammer¹, T.L. Gaarden³, K. Engedal⁴, T. K. Kvien¹, I.K. Haugen¹. ¹Departement of Rheumatology; ²National Advisory Unit on Rehabilitation in Rheumatology; ³Departement of Geriatric Psychiatry, Diakonhjemmet Hospital, Oslo; ⁴Norwegian Advisory Unit of Ageing and Health, Vestfold County Hospital, Tønsberg, Norway

Background: Pain is the most preferred area of improvement for patients with hand osteoarthritis (OA). Whereas only weak associations have been found between radiographic OA severity and pain, few studies have explored whether psychological factors are associated with pain.

Objectives: To examine whether radiographic severity, depression, anxiety and pain catastrophizing are associated with self-reported pain in patients with hand OA, and to explore possible interactions between psychological factors and radiographic severity.

Methods: The Nor-Hand study is an observational cohort study of 300 (89% women) hand OA patients with median (IQR) age of 61 [57–66] years. Participants completed questionnaires, including Numeric Rating Scale (NRS, 0–10 scale) about hand pain, Australian/Canadian (AUSCAN) hand pain subscale (0–20 scale), Hospital Depression and Anxiety Scale (HADS, 0–42 scale) and Pain