massive intimal hyperplasia compared to TABs with mild intimal hyperplasia ($p = 0.01$).

Conclusion: Based on the expression of markers of inflammation and tissue remodeling, different subsets of infiltrating macrophages can be distinguished. Macrophages in vascular lesions of GCA patients display a distinct spatial distribution pattern within the inflamed vessel wall (Figure 1). Adventitial macrophages express highest level of pro-inflammatory cytokines indicating pro-inflammatory functions of these macrophages. Colocalization of CD206 and MMP-9 along media borders indicates a role for CD206+ macrophages in collagen digestion and angiogenesis. Additionally, the association of increased numbers of FR- β + macrophages with extensive intimal hyperplasia suggests that FR- β + macrophages promote myofibroblast proliferation.

REFERENCE

- [1] Watanabe R, Maeda T, Zhang H, Berry GJ, Zeisbrich M, Brockett R, Greenstein AE, Tian L, Goronzy JJ, Weyand CM. MMP (Matrix Metalloprotease)-9-Producing Monocytes Enable T Cells to Invade the Vessel Wall and Cause Vasculitis. *Circ Res*. 2018 Aug 31;123(6):700-715.

Disclosure of Interests: William Febry Jiemy: None declared, Yannick van Sleen: None declared, Annemieke Boots Grant/research support from: grant from MSD in 2010-2015, Consultant for: I was a consultant for Grunenthal Germany 2016-2017, Employee of: I was an employee of Organon, Shering-Plough and MSD from 1991-2011, Riemer Slart: None declared, Peter Heeringa: None declared, Elisabeth Brouwer Speakers bureau: Dr. Brouwer as an employee of the UMCG received speaker fees and consulting fees from Roche which were paid to the UMCG
DOI: 10.1136/annrheumdis-2019-eular.4621

SAT0233 VALIDATION OF A NOVEL DISEASE CLASSIFICATION IN HACETTEPE TAKAYASU ARTERITIS COHORT

Ertuğrul Çağrı Bölek, Selcan Demir, Alper Sari, Ummusen Kaya Akca, Levent Kiliç, Ali Akdoğan, Sedat Kiraz, Omer Karadag, Seza Özen, Hacettepe University Vasculitis Center (HUVAC). *Hacettepe University Vasculitis Center, Ankara, Turkey*

Background: Takayasu Arteritis (TAK) is a rare idiopathic granulomatous large vessel vasculitis and it is a clinically heterogeneous disease. Various classifications and subsets which based on distribution of arterial lesions were defined in the literature in order to exhibit and predict different disease courses.

Objectives: We aimed to validate a new disease subsets developed by Goel et al in our TAK series (1).

Methods: We retrospectively evaluated the medical records of 164 TAK patients followed at Department of Rheumatology and Department of Pediatric Rheumatology in Hacettepe University, Ankara, Turkey between August 2005 and October 2018. The pediatric-onset (< 18 years of age at disease diagnosis) and adult-onset patients fulfilled the Ankara 2008 and the American College of Rheumatology (ACR) 1990 criteria for TAK, respectively. All patients were assigned to three clusters (Cluster 1: Abdominal Predominant, Cluster 2: Aortic Arch Predominant, Cluster 3: Focal Disease) using a decision tree defined in the original study (1). Demographics, clinical and laboratory features, treatment regimens were compared between in three groups.

Results: There were forty-two (25.6%), sixty-three (38.4%) and fifty-nine (36%) patients in Cluster 1, 2 and 3, respectively. Demographic and clinical data was summarized in Table-1. Cluster 1 included approximately half of patients (45.8%) with pediatric-onset TAK ($p = 0.048$). Baseline acute phase reactants (Erythrocyte Sedimentation Rate:ESR and C-reactive protein:CRP) and age at disease diagnosis were slightly lower in Cluster 1, however none of them did not reach statistical significance ($p = 0.94$, $p = 0.99$ and 0.56 , respectively). In contrast, cerebrovascular accident rates were slightly higher in Cluster 2 ($p = 0.24$). Although anti-TNF biological agents were more frequently used for treatment in Cluster 1 ($p = 0.004$), cyclophosphamide and/or overall biological agents usage was similar in three groups ($p = 0.15$).

Conclusion: Decision tree which defined by Goel et al. was applied to our single center pediatric and adult TAK cohort. In contrast to original validation cohorts, there was no difference among three clusters of our cohort except pediatric-onset disease and anti-TNF usage. Dissimilarities among the cohorts in terms of new classification system may be caused either number of patients or ethnic/regional differences.

REFERENCE

- [1] Goel R, Gribbons KB, Maksimowicz-McKinnon K, Hoffman GS, Kumar S, Joseph G, et al., editors. *Discovery and Validation of Novel Disease*

Subsets in 806 Patients with Takayasu's Arteritis across Four International Cohorts. *ARTHRITIS & RHEUMATOLOGY*; 2018: WILEY 111 RIVER ST, HOBOKEN 07030-5774, NJ USA.

Table 1. Demographics and Clinical Features of TAK Disease Clusters

	Cluster 1 (n=42) (Abdominal Predominant)	Cluster 2 (Aortic Arch Predominant) (n=63)	Cluster 3 (Focal Disease) (n=59)	P
Female, n (%)	37 (88.1)	58 (90.1)	53 (89.8)	0.791
Age at TA diagnosis, years, Mean $\pm$ SD	29.3 $\pm$ 15.5	32.0 $\pm$ 13.7	32.6 $\pm$ 13.8	0.56
Pediatric-Onset (< 18 years of age at disease diagnosis)	11 (26.1)	7 (11.1)	6 (10.2)	0.048
Median disease duration, years (IQR)	4.5 (5.1)	5.2 (6.8)	4.9 (6.9)	0.83
Median ESR at TA diagnosis, mm/h (IQR)	48.5 (59)	53.0 (59.0)	62.0 (49.0)	0.94
Median CRP at TA diagnosis, mg/dL (IQR)	2.4 (10)	3.8 (9.0)	3.6 (8)	0.99
Hypertension (HT), n (%)	18 (42.9)	17 (27)	15 (25.4)	0.13
Cerebrovascular Accident (SVA), n (%)	3 (7.1)	11 (17.5)	6 (10.2)	0.24
Death, n (%)	3 (7.1)	2 (3.2)	2 (3.4)	0.56
Methotrexate, n (%)	22 (52.4)	38 (60.3)	34 (57.6)	0.72
Azathiopurine, n (%)	16 (38.1)	18 (28.6)	19 (32.2)	0.59
Leflunomide, n (%)	4 (9.5)	5 (7.9)	2 (3.4)	0.42
Cyclophosphamide, n (%)	19 (45.2)	27 (42.9)	18 (30.5)	0.24
Interleukin-6 blockade, n (%)	9 (21.4)	14 (22.2)	10 (16.9)	0.75
TNF- α inhibitors, n (%)	13 (31.0)	7 (11.1)	5 (8.5)	0.004
Cyclophosphamide and/or biologics, n (%)	27 (64.3)	37 (58.7)	27 (45.8)	0.15
Endovascular intervention*, n (%)	8 (19)	3 (4.8)	7 (11.9)	0.069
Vascular surgery*, n (%)	4 (9.5)	10 (15.9)	4 (6.8)	0.26

Disclosure of Interests: Ertuğrul Çağrı Bölek: None declared, Selcan Demir: None declared, Alper Sari: None declared, Ummusen Kaya Akca: None declared, Levent Kiliç: None declared, Ali Akdoğan: None declared, Sedat Kiraz: None declared, Omer Karadag: None declared, Seza Özen Consultant for: Seza Özen is receiving consultancy fees from Novartis, Speakers bureau: Roche

DOI: 10.1136/annrheumdis-2019-eular.6034

SAT0234 RNA SEQUENCING IDENTIFIES AN IGA VASCULITIS ASSOCIATED SERUM MICRORNA SIGNATURE, DISCRIMINATING PATIENTS WITH IGA VASCULITIS FROM AGE- AND SEX-MATCHED HEALTHY SUBJECTS

Alojzija Hocevar^{1, 2}, Katja Lakota, Thomas Grentzinger³, Alexis Sarazin³, Neža Brezovec¹, Tadeja Kuret^{1, 4}, Oliver Distler⁵, Sasa Cucnik^{1, 4}, Olivier Voinnet³, Snežna Sodin-Semrl^{1, 2}, Matija Tomšič^{1, 6}, Mojca Frank-Bertoncelj⁵. ¹University Medical Centre Ljubljana, Department of Rheumatology, Ljubljana, Slovenia; ²University of Primorska, FAMNIT, Koper, Slovenia; ³Swiss Federal Institute of Technology (ETH Zurich), Zurich, Switzerland; ⁴University of Ljubljana, Faculty of Pharmacy, Ljubljana, Slovenia; ⁵University Hospital Zurich, Center of Experimental Rheumatology, Department of Rheumatology, Schlieren, Switzerland; ⁶University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia

Background: Immunoglobulin A vasculitis (IgAV) is a small vessel vasculitis with IgA deposits in the vessel wall, manifesting with skin purpura, arthralgia/arthritis, gastrointestinal (GI) and renal complications. Altered serum miRNA signatures can reflect disease-specific pathology, which makes serum miRNAs promising disease biomarkers. We have recently reported that miRNA expression is changed in the affected skin of IgAV patients. The profile of serum miRNAs in IgAV, however, remains unknown.

Objectives: To determine the serum miRNA signatures in adult patients with IgAV as compared with healthy controls (HC) and explore *in silico* their gene targets and pathways.

Methods: Small RNA were isolated from sera of IgAV patients with high disease activity (sera collected at the time of diagnosis) and from the age- and sex-matched HC (n=6 each). Small RNA libraries were sequenced with Illumina technology and reads were mapped onto human genome (GRCh38). One IgAV sample was omitted from analysis due to too low number of recovered miRNA reads. Unsupervised clustering was based on the expression of 150 miRNAs with the highest variance across samples. The miRrort platform was used to predict gene targets of differentially expressed (DE) miRNAs with log2 fold change $\geq |1|$ and $p_{adj} < 0.01$. The STRING protein networks platform was used for pathway enrichment analysis of these genes.

Results: Unsupervised clustering of serum miRNA reads clearly distinguished between IgAV patients and HC (Figure 1). Among 1918 annotated miRNA (miRBase), 446 miRNAs were detected in serum samples and 88 miRNAs were identified as DE between IgAV patients and HC (log2 fold change $\geq |1|$, $p_{adj} < 0.05$). Specifically, 28 miRNAs were elevated in the serum of IgAV patients (e.g. miRNA-22, -146a, -185, -320a/

Figure 1. Heatmap based clustering analysis of serum miRNA expression

Figure 2. STRING Protein networks of gene targets of DE miRNAs

b/c, -378a, -423, -3184; $p_{adj} < 10^{-10}$), whereas 60 miRNAs were decreased (e.g. miRNA-128, -937, -30c, -328, -26a, $p_{adj} < 0.005$), thereby representing the IgAV-associated serum miRNA signature. The miRor platform identified 426 protein-coding genes as targets of the 54 DE miRNAs ($\log_2$ fold change $\geq |1|$, $p_{adj} < 0.01$). As analyzed by STRING, these miRNA target genes were enriched in distinct molecular networks and biological pathways, including "Phosphoproteins (FDR 7.4×10^{-5})", "Alternative splicing" (FDR 2.8×10^{-4}), "Regulation of actin cytoskeleton" (FDR 0.008), "Proteoglycans in cancer" (FDR 0.009) and "Fc gamma receptor dependent phagocytosis" (FDR 0.01) (Figure 2). Additionally, miRNA gene targets formed three distinct molecular clusters, specifically "Chemokines and their receptors", "Ubiquitination process" and "Vesicle, endocytosis, lysosomes and their trafficking" (Figure 2). This suggests that the altered miRNAs in IgAV regulate diverse cellular functions, reflecting or contributing to the key aspects of disease pathogenesis.

Conclusion: Here we report for the first time an IgAV-associated serum miRNA signature. The altered miRNAs clearly discriminate IgAV patients from HC, and might play a key role in the pathogenesis of IgAV. Our study sets the basis for the identification of novel, serum-based disease biomarkers in vasculitis.

Disclosure of Interests: ALOJZIJA HOCEVAR: None declared, Katja Lakota: None declared, Thomas Grentzinger: None declared, Alexis Sarazin: None declared, Neža Brezovec: None declared, Tadeja Kuret: None declared, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Italfarmaco, iQvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he had/had consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders, Sasa Cucnik: None declared, Olivier Voinnet: None declared, Snežna Sodin-Semrl: None declared, Matija Tomšič: None declared, Mojca Frank-Bertoncelj: None declared

DOI: 10.1136/annrhumdis-2019-eular.6874

SAT0235

BIOLOGICAL THERAPY IN NEUROBEHÇET. MULTICENTER STUDY OF 29 PATIENTS

José Luis Martín-Varillas¹, Iñigo González-Mazón¹, Belén Atienza-Mateo¹, Monica Calderón-Goercke¹, D. Prieto-Peña¹, Lara Sánchez Bilbao¹, Vanesa Calvo-Río¹, Santos Castañeda², Esther Vicente², Olga Maiz³, Clara Moriano⁴, Elvira Díez Álvarez⁴, José Luis Andréu Sánchez⁵, Concepción Delgado Beltrán⁶, Marta Loreda Martínez⁶, J. Narváez⁷, Angel Ramos Calvo⁸, Francisca Sivera⁹, Enrique Raya¹⁰, Norberto Ortego¹⁰, Jose Luis Callejas-Rubio¹⁰, Anahy Brandy-García¹¹, Alejandro Olive¹¹, Sabela Fernández¹², Ricardo Gómez de la Torre¹³, Ignacio Torre-Salaberri¹⁴, Julio Sánchez¹⁵, Ana Urruticoechea-Arana¹⁶, Eva Salgado-Pérez¹⁷, Rafael Melero¹⁸, Olga Martínez González¹⁹, Susana Romero-Yuste²⁰, Miguel A. González-Gay¹, Ricardo Blanco¹. ¹H.U.M. Valdecilla, Santander, Spain; ²H. La Princesa, Madrid, Spain; ³H. Donosti, San Sebastián, Spain; ⁴H. de León, León, Spain; ⁵H. Puerta de Hierro, Madrid, Spain; ⁶H. Lozano Blesa, Zaragoza, Spain; ⁷H. Bellvitge, Barcelona, Spain; ⁸H. de Soria, Soria, Spain; ⁹H. de Elda, Alicante, Spain; ¹⁰H. San Cecilio, Granada, Spain; ¹¹H. Germans Trias i Pujol, Barcelona, Spain; ¹²H. San Agustín, Avilés, Spain; ¹³H.U.C. Asturias, Oviedo, Spain; ¹⁴H. Basurto, Bilbao, Spain; ¹⁵H. 12 de Octubre, Madrid, Spain; ¹⁶H. Can Misses, Ibiza, Spain; ¹⁷H. Ourense, Ourense, Spain; ¹⁸H. Vigo, Vigo, Spain; ¹⁹H. Salamanca, Salamanca, Spain; ²⁰H. Pontevedra, Pontevedra, Spain

Background: Behçet's disease (BD) is a variable vessel vasculitis and typically presents with mucocutaneous involvement. However, any organ can be affected, being the neurological affection (neurobehçet, NB) one of the most serious manifestations.

Objectives: Our aim was to assess the efficacy and safety of biological therapy as treatment of NB.

Methods: We set up a multicenter observational study of 29 patients with NB on treatment with biological therapy (BT). NB diagnosis was made by neuroimaging, CSF analysis and/or suggestive clinical signs of central and/or peripheral nervous system involvement, excluding infectious causes or more prevalent pathology. Results are expressed as mean $\pm$ SD or as median and interquartile range (IQR) as appropriate.

Results: 29 patients (15 σ /14 ϕ) with an average age of 39.6 ± 10.5 years. HLA-B51 was positive in 48.3% of the patients. Table shows the non-neurological manifestations. Regarding the neurological manifestations, 23 patients (79.3%) had parenchymal involvement (hemiparesis (n=6),