

and serum HMGB-1 level; whereas, we found a positive correlation with both BDCAF and BSAS². This suggests that HMGB-1 can be used as a new disease activity parameter in BS. In conclusion, this study is unique as it involves the largest number of BS patients and uses BDCAF and BSAS together to assess disease activity

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AB0496

AUTOANTIBODIES TARGETING COMPLEMENT RECEPTORS 3A AND 5A1 ARE DECREASED IN ANCA-ASSOCIATED VASCULITIS AND CORRELATE WITH HIGHER RELAPSE RATE.

S. Klapa¹, A. Müller², A. Koch³, A. Kerstein-Staehle², W. Kaehler³, H. Heidecke⁴, S. Schinke², M. Huber-Lang⁵, M. Nitschke⁶, S. Pittann², C. Karsten⁷, G. Riemekasten², P. Lamprecht². ¹University of Lübeck and Institute of Experimental Medicine, Christian-Albrechts-University of Kiel c/o German Naval Medical Institute, Department of Rheumatology and Clinical Immunology, Lübeck, Germany; ²University of Lübeck, Department of Rheumatology and Clinical Immunology, Lübeck, Germany; ³Institute of Experimental Immunology, Christian-Albrechts-University Kiel, c/o German Naval Medical Institute, Kronshagen, Germany; ⁴CellTrend GmbH, Luckenwalde, Luckenwalde, Germany; ⁵Institute of Clinical and Experimental Trauma Immunology, University Hospital Ulm, Ulm, Germany; ⁶Department of Internal Medicine I, Transplant Center, University of Lübeck, Lübeck, Germany; ⁷Institute of Systemic Inflammation Research, University of Lübeck, Lübeck, Germany

Background: Activation of the alternative and final common pathways have been shown in ANCA-associated vasculitis (AAV) (1). Circulating titers of C5a are elevated and correlate with disease activity in AAV. Binding to the corresponding G protein-coupled receptor (GPCR) C5aR1 enhances the influx of neutrophils, leading to ROS generation and severe necrotizing of vascular walls (2). Moreover, subsequent interaction of C5a with C5aR1 may represent a proinflammatory amplification loop (3). Blocking of the receptor is protective in a murine model in AAV (4). In humans, avacopan, a C5aR1-inhibitor showed promising results as glucocorticoid-sparing agent in two randomized phase II and one ongoing phase III clinical trials in AAV (NCT02994927). Notably, disease-specific anti-GPCR autoantibody (aab) signatures have been found in different autoimmune diseases (5).

Objectives: The aim of the present study was to examine whether (patho)physiological anti-C3aR and anti-C5aR1 aabs correlate with clinical findings in AAV, and whether this is linked to the clinical outcome.

Methods: Sera and plasma of AAV patients [granulomatosis with polyangiitis (GPA), n=64; microscopic polyangiitis (MPA), n=26; eosinophilic granulomatosis with polyangiitis (EGPA), n=11] were measured by Elisa for circulating autoantibodies against complement receptors C3a (anti-C3aR aab) and C5a (anti-C5aR1 aab) and plasma levels of C3a and C5a. Expression of C3aR and C5aR1 on T-cells was determined using flow cytometry. Clinical data were assessed at the time of serum sampling and during follow-up for 48 months

Results: GPA displayed low titers of anti-C3aR aab (GPA:5.33±2.54 vs. HD:6.47±2.61, P=0.0031). Anti-C5aR1 aab were decreased in AAV, especially in GPA (GPA:1.02±1.07 vs. HD:6.63±2.91, P<0.0001). Plasma levels of C5a and anti-C5aR aab yielded an inverse correlation in AAV (r=-0.6813, P=0.0127). C5aR1 expression was increased on T-cells in GPA (CD4+C5aR1+T-cells: GPA:10.76±2.55% vs. HD:3.44±0.68%, P=0.0021; CD8+C5aR1+T-cells: GPA:9.74±2.10% vs. HD:4.11±0.92%, P=0.0198). Reduced titers of anti-C5aR1 aab <0.45U/ml displayed an increased relapse risk for major organ involvement in GPA (HR 12.85, P=0.0014).

Conclusion: As potential diagnostic marker, anti-C5aR1 aab titer may additionally be useful to monitor disease activity in AAV.

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AB0497

RENAL INVOLVEMENT IN ANCA-ASSOCIATED VASCULITIS: DO THE PRESENCE OF ANCA AND THEIR TYPE MATTER?

N. Bulanov¹, E. Stolyarevich², A. Zykova^{1,3}, E. Safonova³, E. Shchegoleva¹, E. Kuznezova¹, M. Bulanova⁴, P. Novikov¹, S. Moiseev^{1,3}. ¹Sechenov First Moscow State Medical University, Tareev Clinic of Internal Diseases, Moscow, Russian Federation; ²A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow, Russian Federation; ³Lomonosov Moscow State University, Moscow, Russian Federation; ⁴Vladimir Regional Clinical Hospital, Vladimir, Russian Federation

Background: The role of ANCA type is well established for the risk of relapses of ANCA-associated vasculitis (AAV). However their association with renal involvement and its outcomes is less well understood.

Objectives: To assess clinical and morphological features of ANCA-associated glomerulonephritis (ANCA-GN) and renal survival in ANCA-negative patients, proteinase-3-ANCA (pr3-ANCA) positive and myeloperoxidase-ANCA (MPO-ANCA) positive patients.

Methods: We enrolled 53 patients with AAV, diagnosed according to Chapel Hill Consensus Conference (2012) definition and/or ACR (1990) criteria, with histologically proven renal involvement. There were 13 (24.5%) males, median age at onset was 48 (33; 57) years. Seven patients were ANCA-negative (13.3%), 17 (32.0%) patients were pr3-ANCA positive and 29 (54.7%) patients were MPO-ANCA-positive. ANCA-associated glomerulonephritis (ANCA-GN) class was established according to Berden et al classification.¹ We retrospectively assessed ANCA renal risk score (ARRS) at disease onset.² Twelve patients (22.6%) developed end-stage renal disease (ESRD) after a median of 12 (6.5; 28) months. Renal survival rates were assessed by Kaplan-Meier method and compared by log-rank test.

Results: The only significant difference was median BVAS score which was significantly higher in pr3-ANCA-positive (18 (17;20)) than in MPO-ANCA positive patients (15 (12; 18), p=0.012). Creatinine levels, eGFR, percentage of glomeruli with crescents, global sclerosis, and interstitial fibrosis and tubular atrophy didn't depend on the presence of ANCA or type of the antibodies. The proportion of patients with focal, crescentic, mixed of sclerotic class of ANCA-GN was similar in all groups. There was no significant difference in the numbers of patients with low, medium or high risk of ESRD according to ARRS. One- and three-year renal survival rates were similar in ANCA-negative (81.7% and 60.0% respectively) and ANCA-positive patients (84.2% and 74.6% respectively, Figure 1A). One-year and three-year survival rates were higher in MPO-ANCA-positive (84.4% and 84.4% respectively) than in pr3-ANCA-positive patients (73.1% and 50.1% respectively), however the difference was not statistically significant (Figure 1B).

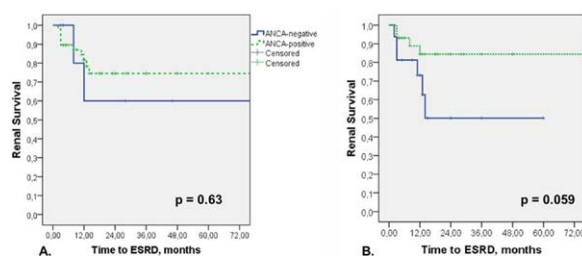


Figure 1. Kaplan-Meier curves showing renal survival in ANCA-positive and ANCA-negative patients (A), and pr3-ANCA-positive and MPO-ANCA-positive patients (B)

Conclusion: Our small study indicates that clinical and morphological features of renal involvement, as well as renal survival are similar in ANCA-negative and ANCA-positive patients and don't depend on the type of ANCA.

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AB0498

CHARACTERISTICS AND OUTCOME OF CORONARY ARTERY LESIONS DUE TO POLYARTERITIS NODOSA: ANALYSIS OF A SINGLE CENTER COHORT IN CHINA

C. Lai¹, L. Zhao², J. Zhou³, D. Xu³, X. Tian³, X. Zeng³, F. Zhang³. ¹Peking Union Medical College Hospital, Beijing, China; ²The Second Hospital of Dalian Medical University, Liaoning, China; ³Peking Union Medical College Hospital, Beijing, China

Background: Polyarteritis nodosa (PAN) is a systemic necrotizing vasculitis that mainly affects medium-sized muscular arteries. The coronary artery could be affected. Some severe cases can lead to spontaneous coronary artery dissection (SCAD) and about 0.02% will die abruptly. Early diagnosis will improve prognosis, but relative studies are all case reports so far.

Objectives: To investigate the clinical characteristics, risk factors and outcome of patients with polyarteritis nodosa (PAN) complicated with coronary artery lesions in China.

Methods: Data of 158 patients with PAN who were admitted to Peking Union Medical College Hospital from September 1986 to September 2019 were retrospective collected. Data were analyzed and compared according to with and without coronary artery lesions due to PAN.

Results: 17 (10.8%) patients with PAN had the coronary artery lesions due to PAN. The age at coronary artery lesion was 36.9±10.3 years. 12 (70.6%) patients were male. There are not statistical differences between two groups in common risk factors of coronary arterial atherosclerosis including smoking, hypertension, diabetes mellitus and hyperlipidemia. Most of them are multi-vessel lesions (8 cases are triple-vessel lesions and 3 cases are bi-vessel lesions). Type of coronary artery affected is shown mainly in stenosis (13 cases). Myocardial infarction are shown in 8 cases (47.1%). Compared to patients without coronary artery lesions, patients with coronary artery lesions had less nervous system involvement (17.6% vs.46.8%) and elevated number of leukocyte (17.6% vs.56%). Besides, patients with coronary artery affected exhibit more cranial and carotid artery involvement(29.4% vs. 5.0%), renal artery involvement (41.2% vs.17.0%), coeliac artery involvement (58.8% vs.27.0%), new onset hypertension (47.1% vs.14.5%), renal infarction (27.3% vs.5.4%), and higher proportion of 2009 Five-factor score (FFS)≥2 (62.5% vs.15.6%). All patients with coronary artery lesions received at least moderate dose of prednisone and CTX except one refused medication. 3 cases underwent interventional therapy. Stent placement was performed on 2 of them, and in-stent stenosis was appeared in a patient one year later. 2 cases died, one for vascular rupture after coronary aneurysms true plus coronary artery bypass grafting, another for myocardial infarction after stopping immunosuppressant therapy himself. Survival analysis showed patients with digital gangrene had poor prognosis though no significant difference (p=0.055).

Conclusion: PAN with coronary artery lesions are not uncommon. These patients exhibit young age, more proportion of multi-vessel of coronary artery involvement, more combined involvements of other organ arteries and more severe disease.

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AB0499

ABNORMALITY OF PERIPHERAL LYMPHOCYTE SUBSETS IN BECHET'S DISEASE AND EFFECTS OF NEW IMMUNOREGULATORY COMBINATION THERAPIES ON THESE CELLS

Q. Y. Su¹, S. X. Zhang², L. M. Hao², J. Y. Yang¹, J. Bai¹, S. J. Guo¹, J. Luo², G. Y. Liu², C. Gao³, X. Li². ¹Shanxi Medical University, Taiyuan, China; ²the Second Hospital of Shanxi Medical University, Taiyuan, China; ³Brigham and Women's Hospital, Harvard Medical School, Boston, United States of America

Background: Bechet's disease (BD) is a chronic multisystemic vasculitis. Although its exact etiopathology is unknown, both autoimmune imbalances associated with genetic and abnormal immune response of effector lymphocytes promoted by infectious factors are suggested¹. The increase of effector T cells (Teffs) and the decrease of regulatory T cells (Tregs) are possibly the involving factors in the pathogenesis of BD². Importantly, we have developed new immunoregulatory combination therapies trying to restore the reduction of Tregs in rheumatic patients.

Objectives: To examine abnormal levels of lymphocyte subsets in BD patients at a relatively large-sample size and to investigate whether the immunoregulatory combination therapies have therapeutic efficacy in BD.

Methods: Total 384 BD patients and 206 healthy controls (HCs) were enrolled in this cross-sectional study. Proportions and absolute numbers of peripheral T, B, NK, CD4⁺ T, CD8⁺ T, Th1, Th2, Th17 and Treg subsets were analyzed by flow cytometry (FCM) for all participants. Among these patients, 183 cases of BD patients were treated with immunoregulatory combination drugs (IMiDs) such as low-dose interleukin-2, rapamycin, metformin, retinoic acid and coenzyme Q10. The levels of peripheral lymphocyte subsets were measured before and after the treatment. Compared-T test was used to compare continuous measures and to assess effect of these drugs.

Results: Compared to HCs, the absolute numbers of various Teffs such as T, B, CD4⁺ T, CD8⁺ T, Th1 and Th17 cells were significantly increased in BD group (P<0.01), while the level of Tregs in patients with BD was severely decreased (P<0.05), resulting in increased ratios (imbalance) of Th1/Tregs, Th2/Tregs and Th17/Tregs (P<0.05) (Figure 1). After the IMiDs treatment, the levels of NK, CD4⁺ T, CD8⁺ T, Th1, Th17 cells as well as Tregs were significantly increased (P<0.05). But the increased Tregs was much more dramatical than those of Teffs, resulting in a decrease in ratios of Teffs/Tregs such as Th2/Tregs (P<0.001) (Figure 2).

Conclusion: Impaired balance of pro- and anti-inflammatory immune cells, especially insufficiency of Tregs, might be a cornerstone of the pathogenesis of BD. Immunoregulatory combination therapies could promote the proliferation and functional recovery of Tregs in patients with BD and might help to alleviate disease activity.

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