mononuclear cells (PBMC) and vascular cells thus obtained were co-cultured for 7 days in different conditions. Vascular cells were cultured in the presence or absence of IFN-γ and tumor necrosis factor alpha (TNF-α) or interleukin-6 (IL-6). Whole blood cultures were incubated at 37°C for 72 hours. When cells reached confluence, they were cultured alone or with allogenic PBMC activated with anti-CD3/CD28 microbeads. After 7 days of culture, cells were separated with a treatment with EDTA and studied by flow cytometry.

Results: Confocal microscopy analyses of GCA arteries showed that neo-intima was mainly composed of myofibroblasts (MF) (α-SMA, Desmin, vimentin, CD34) in contact with CD45 cells and that MF expressed HLA-DR, the phosphorylated form of STAT1 (pSTAT1) and in a lesser extent pSTAT3, strongly suggesting the activation of the IFN-γ signaling pathway rather than the IL-6 pathway. The phenotype of cultured vascular cells isolated from fresh TAB was consistent with MF. When MF were exposed to IFN-γ and TNF-α in vitro, their proliferation capacity decreased and their levels of expression of HLA-DR and CD86 increased (median fluorescence intensity [MFI]) from 0 to 57 (p<0.03) and from 34 to 103 (p=0.03), respectively. In addition, co-cultures of MF and activated PBMC revealed that MF maintained the polarization of T cells into Th1 and Tc1 cells (p<0.001) and to a lesser extent into Th17 and Tc17 cells (p=0.03). This effect was even more significant when MF were previously exposed to IFN-γ and TNF-α but not when they were exposed to IL-6.

Conclusion: Our results show that myofibroblasts are present in the neo-intima of GCA patients and that these MF activate signaling pathways indicative of IFN-γ exposure. Moreover, these MF, especially when exposed to IFN-γ, maintain the polarization of T cells into Th1 and Tc1 cells, which contributes to amplify the production of IFN-γ and thus initiate a pro-inflammatory amplification loop that likely participates in vascular inflammation and remodelling.

REFERENCES:

Disclosure of Interests: None declared


POS0253 PERSONALIZED RISK EVALUATION FOR OUTCOME PREDICTION OF ANCA ASSOCIATED VASCULITIS (AAV) USING LATENT CLASS ANALYSIS AND MACHINE LEARNING.

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Background: ANCA associated vasculitides (AAV) are a heterogeneous group of rare diseases with unknown etiology. In the most severe cases AAV can lead to end stage kidney disease or death. Since etiology and detailed pathogenesis of AAV is not known, the prediction of disease outcome at the time of diagnosis is challenging. Thus, there is an unmet need for tools to identify patients with the highest risk of organ dysfunction and death and apply effective personalized therapy.

Objectives: The aim of this work was to search for tools allowing outcome prediction at the time of AAV diagnosis. Early identification of patients, who are likely to develop severe organ dysfunction and death is crucial for appropriate disease management. Induction therapy in AAV relays on immunosuppressive drugs characterized by a high risk of severe side effects. Thus, their administration in high doses should be limited only to individual patients with an especially high risk of poor outcome.

Methods: We applied here two methods of identification of AAV patients at risk to develop severe organ dysfunction and death. First method (latent class analysis [LCA] followed by logistic regression) was meant to subcategorize patients and identify a subgroup at subjects at risk to develop chronic renal replacement therapy (CRRT) and death [1]. Second, served to assess individual poor outcome and was based on two machine learning (ML) classifiers, which by analyzing clinical information allow assigning computed risk for CRRT and death in an individual patient allowing to identify subjects with high risk of chronic replacement therapy (CRRT) and death. We have evaluated a number of different approaches to build the ML models (including logistic regression, support vector machines, random forests), and obtained the best results for the gradient boosting algorithm implementation called LightGBM [2]. It works as a sequential ensemble of so-called weak learners (decision trees) finally combined in a one prediction model. Both analyses were based on retrospective data from Polish national AAV registry (POLVAS) [3] including presently 565 GPA and 135 MPA patients. The parameters used were: demographic data and laboratory parameters, specific organ involvement, ANCA specificity and time between selected stages of the disease.

Results: LCA used on our AAV cohort identified four subphenotypes – three already previously proposed - and revealing a fourth clinically relevant subphenotype. This new subphenotype includes only GPA patients, usually diagnosed at a younger age as compared to other groups, and characterized by multorgan involvement, high relapse rate, relatively high risk of death, but no end-stage kidney disease. Logistic regression analysis revealed significant differences in the risk of CRRT and death between those subphenotypes – the worst prognosis was found for severe MPO AAV. On the other hand, using ML approach we obtained an individual prediction model with potentially relevant clinical performance (ROC AUC of 0.85 for CRRT and 0.82 for death).

Conclusion: We consider results obtained encouraging. They may offer a new insight into AAV course based on data available at diagnosis, and create a solid foundation for potential clinical decision support system.

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POS0254 IMMUNE RESPONSE TO SARS-COV-2 INFECTION IN PATIENTS WITH RHEUMATIC MUSCULOSKELETAL DISEASES: THE MAINSTREAM STUDY

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