

EXPRESSION OF HIF-1A/VEGF/ING-4 AXIS IN PULMONARY SARCOIDOSIS

W. J. Piotrowski¹, J. Kiszalkiewicz², D. Pastuszak-Lewandoska², P. Gorski¹, A. Antczak³, M. Migdalska-Sek², W. Górski¹, K. Czarnecka², D. Domańska², E. Nawrot², E. Brzezińska²

¹Department of Pneumology and Allergy, 1st Chair of Internal Diseases, Medical University of Lodz, Poland; ²Department of Molecular Bases of Medicine, Medical University of Lodz, Poland; ³Department of General and Oncological Pulmonology, Medical University of Lodz, Poland

Angiogenesis/angiostasis regulated by HIF-1A/VEGF/ING-4 axis may be crucial for the course and outcome of sarcoidosis. Overexpression of angiogenic factors (HIF-1A/VEGF) may predispose to chronic course and lung fibrosis, whereas immunoangiostasis (related to an overexpression of inhibitory ING-4) may be involved in granuloma formation in early sarcoid inflammation. We studied gene expression level of HIF-1A, VEGF and ING-4 in BAL cells and peripheral blood (PB) lymphocytes of sarcoidosis patients (n=94), to better understand mechanisms of the disease, and to search for its biomarkers. Relative gene expression level (mean RQ) was analyzed by qPCR. Results were evaluated according to the presence of lung parenchymal involvement (radiological stage I vs. II-IV), acute vs. insidious onset, lung function test (LFT) results, calcium metabolism parameters, % BAL lymphocyte (BALL%), BAL CD4+/CD8+, age and gender. In BALF cells of patients, the ING-4 and VEGF RQ values were increased, while HIF-1A were decreased. In PB lymphocytes all study genes were overexpressed. Higher expression of HIF-1A in PB lymphocytes of patients with abnormal spirometry, and in BALF cells of patients with lung volume restriction was found (U Mann-Whitney test, P<0.05, vs. subgroup with normal spirometry). VEGF gene expression in BAL cells was also higher in patients with abnormal spirometry. Several inverse correlations between VEGF and different LFT parameters were found. Our results are in line with previous data on the role of HIF-1A/VEGF/ING-4 axis in the pathogenesis of sarcoidosis. Upregulated HIF-1A and VEGF genes are linked to acknowledged negative prognostic factors.