TGF-β AND SMADS MRNA EXPRESSION LEVEL IN PULMONARY SARCOIDOSIS.

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Lung fibrosis is a severe complication of sarcoidosis. TGF-β/SMAD signaling pathway may play an important role in this process. We evaluated gene expression of TGF-β, SMAD2, SMAD3 and SMAD7 in bronchoalveolar lavage (BAL) cells and peripheral blood (PB) lymphocytes of patients with sarcoidosis (n=94) to search for diagnostic and prognostic value of these markers. Relative gene expression level (mean RQ) was analyzed by qPCR. The results were analyzed according to the presence of lung parenchymal involvement (radiological stages 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. TGF-β and SMAD3 expressions in patients PB lymphocytes were significantly higher comparing to control group, but there were no difference in BAL cells. Up-regulation of SMAD7 (inhibitory Smad) and down-regulation of SMAD3 in BAL cells in all clinical classification groups were found. Expression of TGF-β in PB lymphocytes was the highest in patients with lung parenchymal involvement and in insidious onset phenotype. The expression of TGF-β in BAL cells was higher in patients with abnormal spirometry (p=0.0124), and TGF-β and SMAD3 in patients with lung volume restriction (p=0.034 and 0.031, respectively). Moreover, several statistically significant negative correlations were found between the expression of SMAD2 and SMAD 3 in BAL cells and various lung function parameters. Based on our results we conclude that TGFβ, SMAD2 and SMAD3 are involved in the pathogenesis of pulmonary sarcoidosis. These biomarkers may have negative prognostic value.