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Title: Cytokine profiles of bronchoalveolar lavage fluid in patients with combined pulmonary fibrosis and emphysema

Dr. Sadatomo 1259 Tasaka tasaka@cpnet.med.keio.ac.jp MD [1], Dr. Kosuke 1260 Mizoguchi sakamotoryoma312ozakiyutaka@gmail.com MD [1], Dr. Yohei 1261 Funatsu dodeko81@ybb.ne.jp MD [1], Dr. Ho 1262 Namkoong hounamugun@gmail.com MD [1], Dr. Wakako 1768 Yamasawa wakako@df6.so-net.ne.jp MD [2], Dr. Makoto 1769 Ishii ishii@z6.keio.jp MD [1], Dr. Naoki 1770 Hasegawa n-hasegawa@z8.keio.jp MD [3] and Prof. Tomoko 1771 Betsuyaku tbetsuyaku@z5.keio.jp MD [1]. [1] Division of Pulmonary Medicine, Keio University School of Medicine, Tokyo, Japan ; [2] Department of Laboratory Medicine, Keio University School of Medicine, Tokyo, Japan and [3] Center for Infectious Diseases and Infection Control, Keio University School of Medicine, Tokyo, Japan .

Body: Background: Combined pulmonary fibrosis and emphysema (CPFE) is characterized by upper lobe emphysema associated with lower lobe fibrosis. Objectives: We aimed to examine whether the cytokine levels in the alveolar space are associated with the development of emphysematous changes that were superimposed on pulmonary fibrosis. Methods: We retrospectively evaluated 102 consecutive patients who were diagnosed with pulmonary fibrosis after bronchoalveolar lavage (BAL). Cytokine levels and differential cell counts in BAL fluid, pulmonary function, CT scores, and levels of serum markers were compared between patients with emphysema and those without. Results: Among the 102 patients (14 females, mean age, 68 y/o), 38 showed upper lobe emphysema on CT. In BAL fluid, the levels of ENA-78/CXCL5 and IL-8/CXCL8 were significantly higher in patients with emphysema than in those without. The levels of MCP-1/CCL2, MIP-1α/CCL3, TNF-α, TGF-β1, and neutrophil elastase did not differ between the two patient groups. In patients with emphysema, whereas %VC was greater, FEV1/FVC and $\%DL_{CO}/V_A$ were lower than in those without emphysema. The composite physiologic index and serum levels of KL-6 and SP-D, markers of interstitial lung disease, were not different between the groups. Levels of CXCL8 and CXCL5 were associated with the proportion or absolute number of neutrophils in BAL fluid. In addition, CXCL8 levels were correlated inversely with %VC and $\%DL_{CO}/V_A$ and positively with the area of low attenuation on CT. Conclusion: Elevated CXC chemokine levels in the airspace might contribute to the emphysematous change in patients with pulmonary fibrosis, which may be associated with the development of CPFE.