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Title: Significance of protein S in patients with interstitial lung disease

Dr. Masahiro 6293 Naito aiaiyuyu@clin.medic.mie-u.ac.jp MD [1], Dr. Osamu 6294 Taguchi taguchio@clin.medic.mie-u.ac.jp MD [1], Dr. Kentaro 6295 Fujiwara kentaro-fu@clin.medic.mie-u.ac.jp MD [1], Dr. Masahiro 6296 Onishi m-onishi@clin.medic.mie-u.ac.jp MD [1], Dr. Takehiro 6297 Takagi takeko@clin.medic.mie-u.ac.jp MD [1], Dr. Tetsu 6298 Kobayashi ktetsu@clin.medic.mie-u.ac.jp MD [1], Dr. Hiroyasu 6299 Kobayashi hirokoba@clin.medic.mie-u.ac.jp MD [1], Dr. Corina 6300 D'Alessandro-Gabazza dalessac@clin.medic.mie-u.ac.jp MD [2] and Prof. Dr Esteban 6316 Gabazza gabazza@doc.medic.mie-u.ac.jp MD [2]. [1] Department of Respiratory Division, Mie University School of Medicine, Tsu, Japan and [2] Department of Immunology, Mie University Graduate School of Medicine, Tsu, Japan .

Body: Background: Protein S exerts anticoagulant activity by acting as a cofactor of activated protein C for the inactivation of coagulation factors Va and VIIIa. We have previously reported that protein S protects against lipopolysaccharide-induced acute lung injury by directly inhibiting the local expression of inflammatory cytokines without affecting coagulation (Takagi T, et al. 2009). However, the role of protein S in interstitial lung disease remains unclear. Objective: The aim of this study is to evaluate the clinical significance of protein S in patients with interstitial lung disease. Methods: This study comprised 106 patients with interstitial lung disease admitted in our institution between August 2008 and December 2011. There were 39 patients with interstitial pneumonia, 25 with sarcoidosis, 9 with collagen vascular disease-associated interstitial lung disease, 8 with organizing pneumonia, 7 with eosinophilic pneumonia, 5 with tumor-associated lung disease, 5 with inflammatory disease, 4 with hypersensitivity pneumonitis, 2 with IgG4 related multi-organ lymphoproliferative syndrome, 1 with alveolar proteinosis, and 1 patient with alveolar hemorrhage. Levels of protein S in BALF were measured using an enzyme-linked immunosorbent assay. Results: Significant changes in the BALF levels of protein S were observed among the different types of interstitial lung diseases. The BALF level of protein S was significantly correlated with the number of macrophages, lymphocytes and with the BALF concentration of total protein and albumin. Conclusion: These results suggest that protein S plays role in the pathogenesis of interstitial lung disease.