Serological diagnosis of idiopathic pulmonary alveolar proteinosis


Previously, we reported the specific occurrence of neutralizing autoantibodies against granulocyte-macrophage colony-stimulating factor (GM-CSF) in the bronchoalveolar lavage fluid from 11 Japanese patients with idiopathic pulmonary alveolar proteinosis (I-PAP). The autoantibody was also detected in sera from all 5 I-PAP patients examined. To determine that the existence of the autoantibody is not limited to the Japanese patients, we examined sera from 24 I-PAP patients in five countries and showed that the autoantibody was consistently and specifically present in such patients. Thus, detection of the autoantibody in sera can be used for diagnosis of I-PAP. To establish a simple and convenient method for diagnosis of I-PAP, we developed a novel latex agglutination test using latex beads coupled with recombinant human GM-CSF. GM-CSF binding proteins isolated from the sera using the latex beads were identified as the autoantibodies of IgG(1) and IgG(2). The titer of the autoantibody determined by this test correlated with that determined by ELISA. Agglutination was positive in 300-fold diluted sera from all 24 I-PAP patients, but negative in sera from four secondary PAP patients, two congenital PAP patients, 40 patients with other lung diseases, and 38 of 40 normal subjects. These results establish that the latex agglutination test is a reliable method for serological diagnosis of I-PAP with high sensitivity (100%) and specificity (98%).