The Diagnostic Value of the Interstitial Biomarkers in Combined Pulmonary Fibrosis and Emphysema

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Abstract

The combined pulmonary fibrosis and emphysema (CPFE) was reported first in 1990, but it has been comparatively underestimated until recently. Although the diagnostic findings of both emphysematous and fibrotic regions are detectable by high-resolution computed tomography (HRCT) of the chest, the degree of progressive fibrosis, which increases with emphysematous lesions, is difficult to evaluate. In this study, we hypothesized that the biomarkers for pulmonary fibrosis, surfactant protein D (SP-D), and KL-6 would serve as good indicators of fibrotic lesions in CPFE. We recruited 46 patients who had been diagnosed in our hospital with both emphysema and fibrosis by their CT scan image from April 2003 to March 2008. The correlation among their pulmonary function tests, composite physiologic index (CPI), and the serum levels of SP-D and KL-6 was evaluated. We found a correlation between KL-6 and %VC, %TLC, or CPI and between SP-D and %VC or CPI. Interestingly, the combined product of KL-6 and SP-D (KL-6xSP-D) was found to highly correlate with %VC and %TLC or CPI. These results show that both KL-6 and SP-D, and especially the product of SP-D and KL-6, are good indicators of the presence of fibrotic lesions in the lungs of CPFE patients. Since the combined pulmonary fibrosis and emphysema was first reported as "combined cryptogenic fibrosing alveolitis and emphysema" by Wiggins et al. in 1990 , the disease has come to be generally recognized worldwide and was listed as "an atypical phenotype of idiopathic interstitial pneumonia" in the 3rd version of the Clinical Guideline for Idiopathic Interstitial Pneumonia, published in 1991 by the Diffuse Pulmonary Disease Group of the Ministry of Health, Labour and Welfare of the Japanese Government. However, the disease was underidentified until 2005, when Cottin et al. reported a retrospective study of 61 patients with both emphysema and pulmonary fibrosis and described the syndrome comprehensively. The diagnosis is based on high-resolution computed tomography (HRCT) of the chest, with findings that indicate emphysema of the upper lobe and pulmonary fibrosis of the lower lobe. CPFE is characterized by a relatively well-preserved lung volume, severely impaired carbon monoxide transfer, significant decrease in PaO2 on exercise, and a high prevalence of pulmonary hypertension leading to a poor prognosis. We expect that the extent of pulmonary fibrosis in CPFE patients might influence the outcome, because patients with CPFE have a worse prognosis than patients with emphysema. However, it is difficult to evaluate the extent of pulmonary fibrosis in patients with CPFE. Vital capacity and DLco are closely influenced by emphysematous change. Wells et al. proposed the composite physiologic index (CPI), calculated from the individual predicted percentage values for VC, DLco, and FEV1.0 as a new indicator of the extent of pulmonary fibrosis, and this index was shown to represent the extent of pulmonary fibrosis on HRCT, adjusting for emphysema.

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