Abstract

Acute exacerbation of idiopathic pulmonary fibrosis has a poor prognosis associated with neutrophilic inflammation. Interleukin-23 is a proinflammatory cytokine involved in neutrophilic inflammation. However, little is known about its role in acute exacerbation of pulmonary fibrosis. This study was performed to determine the role of interleukin-23 in acute exacerbation of pulmonary fibrosis. For assessment of acute exacerbation of pulmonary fibrosis, mice were intratracheally administered bleomycin followed by lipopolysaccharide. Inflammatory cells, cytokine levels, and morphological morphometry of the lungs were analyzed. Cytokine levels were measured in the bronchoalveolar lavage fluid of idiopathic pulmonary fibrosis patients with or without acute exacerbation. Interleukin-23, -17A, and -22 levels were increased in the airway of mice with acute exacerbation of pulmonary fibrosis. Interleukin-23p19-deficient mice with acute exacerbation of pulmonary fibrosis had markedly reduced airway inflammation and fibrosis associated with decreased levels of interleukin-17A and -22 compared with wild-type mice. Treatment with an anti-interleukin-23 antibody attenuated airway inflammation and fibrosis and reduced interleukin-17A and -22 levels in mice with acute exacerbation of pulmonary fibrosis. T helper 17 cells were the predominant source of interleukin-17A in mice with acute exacerbation of pulmonary

fibrosis. Interleukin-23 levels in bronchoalveolar lavage fluid tended to be higher in idiopathic pulmonary fibrosis patients with than without acute exacerbation. The data presented here suggest that interleukin-23 is essential for the development of acute exacerbation of pulmonary fibrosis, and that blockade of interleukin-23 may be a new therapeutic strategy for acute exacerbation of pulmonary fibrosis.

Keywords: idiopathic pulmonary fibrosis, lipopolysaccharide, T-helper type 17 cells, innate lymphoid cells

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